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The American Heart Journal

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Original Communications

THE DEVELOPMENT OF MITRAL STENOSIS IN YOUNG PEOPLE

WITH A DISCUSSION OF THE FREQUENT MISINTERPRETATION OF A MIDDIASTOLIC MURMUR AT THE CARDIAC APEX*†

EDWARD F. BLAND, M.D., PAUL D. WHITE, M.D., AND T. DUCKETT JONES, M.D.
BOSTON, MASS.

A GROSS discrepancy between the clinical diagnosis of rheumatic mitral stenosis and the actual alterations found post mortem has occurred in our experience with sufficient frequency to cause us to study this particular problem. The error in diagnosis has been committed most often in young individuals dying relatively early after the onset of severe rheumatic fever. It became evident as this study progressed that an important source of error was the general unqualified acceptance (in the absence of free aortic regurgitation) of a mid or late rumbling diastolic murmur at the cardiac apex as indicative of mitral valve obstruction (stenosis). Since this murmur may appear during the first few weeks after the onset of rheumatic fever, evidence to be of value in arriving at a correct interpretation of its clinical significance must be obtained largely from post-mortem observation on patients dying at various early intervals after the onset of the disease. Furthermore, it seemed to us probable that this method of approach would contribute considerable information regarding the often repeated question as to the length of time required for the development of important deformity and stenosis of the mitral valve. Previously published reports are of little value in this con-

*From the Massachusetts General Hospital and the House of the Good Samaritan, Boston, Mass. Studies at the latter institution are financed by the Commonwealth Fund, Inc.

†Presented at the meeting of the American Heart Association in Atlantic City, New Jersey, June 11, 1935.

nection since the majority of clinical and pathological studies are concerned largely with older patients and, hence, with long-standing rheumatic valvular disease.

In the present communication we are presenting clinical and post-mortem observations on a group of 100 young individuals with rheumatic heart disease. The series is of sufficient size to warrant certain conclusions as to the evolution of rheumatic valvular disease in general. Special attention has been directed to the development of mitral valve deformity and stenosis. An evaluation of the low pitched rumbling diastolic murmur frequently heard at the cardiac apex and often misinterpreted in such patients is included, together with a discussion of the factors probably responsible for its production.

POST-MORTEM DATA

Our material has been assembled from two sources and consists of the necropsy findings and clinical records of 100 patients twenty-one years of age or younger who showed at post-mortem examination changes in the heart generally attributed to rheumatic fever. Seventy-two of this series constitute the total number which occurred among 7,600 autopsies performed at the Massachusetts General Hospital during the years 1898 to 1935. The remaining twenty-eight represent a similar age group from the necropsy material at the House of the Good Samaritan in Boston, where over 1,200 patients with active rheumatic fever or chorea have received prolonged institutional care and intensive clinical study during the past fifteen years. We have purposely confined the investigation to this special and hence numerically limited group of young people for reasons already discussed. This group also represents the age at which rheumatic fever most frequently occurs and here one may expect a greater degree of accuracy in determining the onset and subsequent course of the disease than is possible in older patients in whom the details of the original infection have been either entirely forgotten or obscured by the passage of years.

A recrudescence of rheumatic infection was the outstanding cause of death in this series and was directly responsible for the fatal issue in eighty-five instances. Postoperative complications accounted for five more deaths, in three of which there was post-mortem evidence of active rheumatic disease also. Subacute bacterial endocarditis caused four deaths, and an acute bacterial endocarditis together with septic disease elsewhere in the body was responsible for three others. Tuberculous meningitis, typhoid fever, and multiple pulmonary abscesses, respectively, killed the remaining three patients. The average age at death for the entire group was thirteen years.

RELATION OF THE DURATION OF THE DISEASE TO THE DEGREE OF MITRAL VALVE DEFORMITY

The interval from the onset of rheumatic fever to death, and the resulting alterations found post mortem in the mitral leaflets have been summarized in Table I. It is to be emphasized that the probable duration as obtained from the clinical records represents a minimal figure, and, where inaccuracies occur, the error is such that the duration of the disease is actually longer than indicated.

TABLE I

STRUCTURAL ALTERATION OF THE MITRAL VALVE AND DURATION SINCE ONSET OF RHEUMATIC FEVER—100 CASES

GROUP	1-6 MO.	6-12 MO.	1-2 YR.	2-5 YR.	5+ YR.	?	TOTAL
I. Deformity with anatomical stenosis	0	1*	2	8	12	0	23
II. Deformity without anatomical stenosis	0	0	7	8	10	0	25
III. Slight thickening, no deformity	4	6	7	6	4	3	30
IV. Fresh vegetations, no thickening or deformity	16	4	0	0	0	0	20
V. No vegetations, no thickening or deformity	0	1	0	0	1†	0	2
Total cases	20	12	16	22	27	3	100

*See text for details about this case.
†Moderate aortic valve deformity.

For the purpose of this study the entire series has been arranged in five groups according to the extent of gross alteration found in the leaflets of the mitral valve. Those instances in which the scarring was extensive enough to produce any actual narrowing of the mitral orifice have been placed in Group I. In Group II we have listed the cases which showed extensive scarring and gross deformity of the valve curtains, but no anatomical stenosis of the orifice. It is of interest that the circumference of the valve ring as measured along the free edge in the majority of this group was actually greater than an arbitrary normal figure of 8.5 cm. However, the degree of mechanical handicap imposed upon the heart appears to have been essentially of the same order in this group as in those patients who had actual stenosis of the orifice. A review of the clinical course and a comparison of the heart weights at necropsy for the two groups support this impression (Table II). Group III on the other hand is composed of those patients who showed on gross examination very slight thickening of the mitral leaflets usually along the free edge without fusion of the cusps but often with minute fresh vegetations. It is probable that in the majority of this group the functional handi-

cap to the heart, directly the result of the valvular deformity, was extremely slight. This is supported by the considerably lighter weight of these hearts as compared with that of Groups I and II. Here and in the subsequent two groups we have reason to believe that the valvular involvement per se played no important rôle in the course of the disease.

TABLE II

COMPARISON OF HEART WEIGHT WITH DURATION AND DEGREE OF MITRAL VALVE DEFORMITY

GROUP	NUMBER CASES	AVERAGE AGE AT DEATH	DURATION SINCE ONSET	HEART WEIGHT (93 CASES)
I. Deformity with anatomical stenosis	23	16 yr.	6.3 yr.	480 (2.0)†
II. Deformity without anatomical stenosis	25	14 yr.	5.0 yr.	470 (2.4)
III. Slight thickening, no deformity	30	14 yr.	2.8 yr.	350 (1.8)
IV. Fresh vegetations, no thickening	20	11 yr.	5.0 mo.	269 (2.0)
V. No vegetations, no thickening	1*	4 yr.	8.0 mo.	200 (2.7)
Total group	99*	13 yr.	3.6 yr.	395 (2.5)

*The case with aortic regurgitation and no mitral valve lesion omitted.
†The figures in parentheses represent weight times normal corrected for age.

In Group IV the only macroscopic evidence of valvular alteration was the presence of an active rheumatic endocarditis manifested by a row of minute pinkish gray vegetations along the line of closure. In this group there was no valvular deformity.

Group V consists of only two patients in whom at necropsy there was no demonstrable change of any sort in the mitral curtains. Each is of unusual interest and worthy of special comment. In the first instance listed in column 2 of Table I, the clinical course was typical of severe rheumatic infection in a boy four years of age. There had been acute arthritis at the onset followed by ill health, cyclic bouts of fever, multiple rheumatic nodules, and finally a severe exacerbation with pericarditis, general venous congestion and death at the end of eight months. Apical systolic and diastolic murmurs usually considered pathognomonic of mitral valve deformity (stenosis and regurgitation) were present throughout the illness. At post-mortem examination the heart showed the usual gross dilatation, but the interesting and surprising finding was an entirely normal appearance of the valve leaflets of all four orifices. Careful scrutiny with a hand lens revealed no gross evidence of disease and no vegetations. Histological sections of the myocardium, however, showed changes typical of severe rheumatic carditis. It is of further interest in this connection that Garber[1] has recently collected from the literature seventeen similar cases of extensive rheumatic myocarditis without gross

evidence of valvulitis, to which he has added another case of his own. We will have occasion to comment upon this patient again in connection with a discussion of the significance of apical diastolic murmurs in the absence of important mitral valve deformity. The second case in this group and listed in column 5 of Table I is of interest in that there were present moderate scarring and deformity of the aortic cusps of rheumatic origin without evident disease of the mitral valve. No mitral diastolic murmur had been heard in this instance.

Of the thirty-two patients who died during the first year after the onset of rheumatic fever the majority (twenty) showed minute verrucose vegetations along the line of closure but no other alteration of the mitral leaflets upon macroscopic examination. In ten instances, and usually toward the end of the first year, there was present in addition to verrucose vegetations slight thickening of the free margins of the mitral curtains associated with some shortening and thickening of the chordae tendineae. Actual deformity, if present, was minimal. The two remaining cases were unusual. One of them has already been commented upon in that no evident valvular involvement was present. The final instance of those who died within the first year is exceptional. Well-marked stenosis of the mitral valve was present. In this instance the clinical record, which appeared to be entirely adequate, indicated no symptoms of ill health prior to the onset of typical rheumatic fever nine months before death. It appears significant, however, that well-marked rheumatic heart disease was present when the patient was examined on the second day after the onset of the symptoms of rheumatic fever. At post-mortem examination the mitral orifice showed advanced stenosis admitting only the tip of one finger. In view of the consistent relationship between the duration of the disease and the resulting valvular deformity for the remainder of this group, it is probable that in this apparently exceptional instance the actual onset of active disease antedated by many months the appearance of clinically recognizable symptoms of rheumatic fever. Of this, however, we have no proof.

It is apparent also from Table I that after the first year and often becoming more extensive during subsequent years the structural alterations of the mitral leaflets assume increasing importance. Although considerable deformity may develop during the second year, scarring of sufficient extent to produce stenosis at the mitral orifice is rarely present before the third year. Thereafter the majority in our series (38 out of a total of 52) had developed valvular deformity either with or without actual stenosis of sufficient extent to contribute a considerable mechanical handicap to the functional capacity of the heart.

INCIDENCE AND EXTENT OF COMBINED VALVULAR LESIONS

Table III indicates the relative frequency of valvular lesions. These pathological findings are in close agreement with the experience of Coombs[2] published in 1924, as well as with the figures of others derived from post-mortem findings in adults. In general it is true that when rheumatic endocarditis is present, the mitral valve is involved. One exceptional instance of aortic without mitral involvement has been noted. When combined with other valvular lesions the mitral involvement is the greatest in extent; later, in adult life, fibrotic changes and calcification may alter this relationship. The association of mitral and aortic valve injury occurred in forty-five instances, or almost half the total series. The mitral, aortic, and tricuspid valves were involved in twenty instances; all four valves were injured five times, while the mitral and tricuspid valves were involved without other valve lesions in five instances.

TABLE III

INCIDENCE OF VALVE INJURY

TOTAL	MITRAL	AORTIC	TRICUSPID	PULMONARY	NONE
100	98	71	31	5	1

Calcium deposits were present in the mitral valve ring in ten instances and were invariably associated with gross deformity, consisting in eight cases of marked stenosis of the orifice. These patients represented an older group, the youngest being fifteen years of age; the average duration from the onset of the disease to the time of death was fifteen years.

From a consideration of the data discussed above and summarized in Table I it is clear (1) that the evolution of the early alterations in the mitral cusps as a result of rheumatic fever follows a consistent course, and (2) that the development of important scarring and deformity of the mitral valve requires a considerable length of time.

CLINICAL OBSERVATIONS ON THE SO-CALLED CHARACTERISTIC SIGNS OF MITRAL STENOSIS

A low pitched rumbling, or less often blowing, murmur in mid-diastole or late diastole (often crescendic in character) heard with maximal intensity in the vicinity of the cardiac apex in the absence of free aortic regurgitation is generally considered indicative of mitral valve obstruction sufficient to warrant a clinical diagnosis of mitral stenosis. Furthermore, the presence of an accompanying diastolic thrill or, if the heart rhythm is normal, of a presystolic thrill ending abruptly with the shock of an accentuated first sound, com-

pletes our clinical concept of the classical signs of the more pronounced cases of this lesion. Austin Flint[3] pointed out in 1862 that occasionally an apical middiastolic or presystolic murmur may be found with free aortic regurgitation in the absence of disease of the mitral valve. In 1923 Wood and White[4] expressed the opinion that "diastolic murmurs may occur in certain large hearts with normal valves and lead to a false diagnosis of mitral stenosis. Left ventricular dilatation of high degree seems to be the main factor in such cases, and may perhaps also explain the Austin Flint murmur which is heard only in certain cases of aortic regurgitation."

It has been enlightening to review the structural alterations found post mortem in those of our cases in which mitral stenosis had been diagnosed clinically. In our total series of 100 cases mitral stenosis (with regurgitation) was considered to be present in sixty-eight instances on the basis of a rumbling mitral diastolic murmur (and of a blowing systolic murmur) best heard at the apex of the heart. In addition to the murmurs, an accompanying diastolic thrill was also present in thirty of this group. No instance of so-called "pure" mitral stenosis was encountered. (See Table IV.)

TABLE IV

COMPARISON OF THE INCIDENCE OF MITRAL DIASTOLIC MURMURS AND THRILLS WITH THE DEGREE OF MITRAL VALVE DEFORMITY

GROUP	NUMBER OF CASES	MITRAL DIASTOLIC MURMUR	MITRAL DIASTOLIC THRILL
I. Deformity with anatomical stenosis	23	21 (91%)	13 (56%)
II. Deformity without anatomical stenosis	25	19 (76%)	8 (33%)
III. Slight thickening, no deformity	30	18 (60%)	4 (13%)
IV. Fresh vegetations, no thickening	20	9 (45%)	5 (25%)
V. No vegetations, no thickening	2	1	0

It is a striking fact that of these sixty-eight cases with mitral diastolic murmurs only twenty-one (less than one-third) actually had anatomical stenosis of the mitral orifice. In nineteen additional cases, however, there were present extensive wrinkling and gross deformity of the cusps but no real stenosis; in fact, frequently the valve circumference was equal to or even greater than normal. The remaining twenty-eight cases had either no deformity or at most minimal thickening of the free margin of the valve curtains. Furthermore, in only two of these twenty-eight instances was there also an incompetence of the aortic valves of sufficient degree to suggest that the mitral diastolic murmur might have been an Austin Flint phenomenon. These figures appear even more significant when one considers that the patients were observed

clinically in two institutions where cardiovascular disease, and especially the rheumatic type, receives intensive and specialized study.

There must exist then other and important factors common to this group which offer a more satisfactory basis for the physical signs of apparent mitral stenosis where such does not actually exist. In each case there was present severe and relatively recent rheumatic infection, and marked cardiac enlargement was evident clinically, together with the common post-mortem findings of an hypertrophied and markedly dilated heart with a flabby ventricular wall and the histological picture of diffuse rheumatic myocarditis. Although the valve rings usually share in the general dilatation, their structure is relatively rigid, and the dilatation of the cardiac cavities is in proportion considerably greater. Whether the true explanation of the signs of apparent mitral stenosis in these cases is that of a relative stenosis of the orifice in relation to the dilated ventricular cavity, or if vibrations set up by the diastolic filling of a capacious cavity with relaxed and relatively atonic walls are responsible for the rumbling murmur and the occasional thrill, or if there is a combination of these factors, we are not prepared to say. Of some interest in this connection is the absence of a comparable diastolic murmur in adults in whom with onset of weakness, dilatation, and failure of the left ventricle following long-standing hypertension, aortic valve disease, or recent coronary thrombosis with myocardial infarction a low dull sound in diastole may occur and give rise to a gallop rhythm. The explanation of this difference is not as yet clear. Furthermore, English physicians in the Indian Medical Service have called attention to the fact that severe ankylostoma (hookworm) infection in native children often results in a severe anemia (1.5 to 2.0 million red cell count) and marked cardiac dilatation accompanied by the signs of congestive heart failure. Typical and pronounced apical systolic and diastolic (presystolic) murmurs often occur in these cases showing marked cardiac dilatation. Upon treatment and cure of the infection the heart returns to normal size and the murmurs completely disappear. Gunewardene[5] in 1933 remarked upon the frequency with which a diagnosis of mitral stenosis has erroneously been made in such instances. In three of his recorded cases the heart returned to normal size, and the murmurs disappeared in response to treatment. In the fourth instance a post-mortem examination revealed a dilated heart with a pale and fatty myocardium but no valvular disease. The author believed a "relative stenosis" was the most likely explanation for the murmurs erroneously interpreted as those of mitral stenosis.

DISCUSSION

It is evident that with severe and recent rheumatic infection in childhood when well-marked cardiac enlargement (dilatation) is

known to have occurred within a few months, the presence of a rumbling sound or short blowing murmur in middiastole or late diastole in the vicinity of the cardiac apex in addition to the usual systolic murmur cannot be considered pathognomonic either of mitral stenosis or of any other extensive valvular deformity, but is dependent fundamentally upon severe myocardial disease. This appears to be true even in the presence of an accompanying diastolic thrill and is further supported by our other data recorded above which indicate that a minimum of two or more years must elapse before important valvular deformity occurs. The presence of minute rheumatic vegetations in most of the early cases suggests, however, that ultimately in the course of several years fibrosis and deformity of the mitral valve might have developed to a sufficient extent to have justified our original (but incorrect) clinical diagnosis at the time of the acute illness.

In addition to these clinically as well as pathologically observed cases, we have encountered thirty-two instances out of a total of 950 patients with rheumatic heart disease who at the time of their acute rheumatic fever showed cardiac enlargement and "mitral diastolic murmurs" which were wrongly attributed to mitral stenosis and regurgitation as previously discussed. Four of this group had a corresponding diastolic thrill in addition to a diastolic rumble. At the present time after an average follow-up period of over eight years since the original infection this group of thirty-two patients have clinically normal hearts without murmurs or enlargement. They doubtless represent clinical counterparts of the occasionally observed pathological instances of rheumatic carditis without valvulitis. Further observations on the regression and disappearance of the physical signs of rheumatic heart disease are now in progress and will be reported at a later date.

It is to be added, however, that an apical middiastolic rumbling murmur, as well as the longer murmur with presystolic accentuation, often does mean real mitral stenosis even in childhood, and in some of our older children mitral stenosis rather than ventricular dilatation was responsible for this murmur. The less the evidence of active infection and of cardiac dilatation, the more significant of mitral stenosis is the mitral diastolic murmur. Especially is this the case in adults.

In closing, it may be suggested that the presence of a mitral middiastolic murmur first appearing from a few days to several months after the onset of an acute rheumatic infection may be taken to mean myocardial rheumatism and left ventricular dilatation and perhaps actually serve as another sign of activity of the rheumatic state.

SUMMARY AND CONCLUSIONS

From a clinical and post-mortem study of 100 young patients it has been shown that:

1. The evolution of rheumatic involvement of the mitral valve follows within limits a consistent course.

2. The ultimate development of extensive valvular deformity either with or without actual stenosis of the mitral orifice probably requires a minimum of two years and in most instances a considerably longer period of time. Exceptional cases have been noted.

3. The significance of a mitral diastolic murmur present during the course of active rheumatic fever has been discussed. Evidence is presented to show that in certain circumstances it is not characteristic of mitral stenosis. Myocardial weakness and ventricular dilatation appear to be responsible in these cases for its production.

REFERENCES

1. Garber, C. Z.: Rheumatic Heart Disease Without Valvulitis, Am. J. Path. 9: 443, 1933.
2. Coombs, C. F.: Rheumatic Heart Disease, New York, 1924, William Wood and Co.
3. Flint, Austin: On Cardiac Murmurs, Am. J. M. Sc. 44: 29, 1862.
4. Wood, J. E., and White, P. D.: The Interpretation of Mitral Diastolic and Aortic Systolic Murmurs, Med. Clin. North America 7: 729, 1923.
5. Gunewardene, H. O.: Cardiac Complications of Ankylostoma Infection With Special Reference to Presystolic Murmurs Occurring in These Cases, J. Trop. Med. 36: 49, 1933.

THE INFLUENCE OF THE HEAT REGULATORY MECHANISM ON RAYNAUD'S DISEASE*†

HERMAN E. PEARSE, JR., M.D.
ROCHESTER, N. Y.

RAYNAUD, in the description of the disorder‡ that bears his name, ascribed its etiology to "a fault of vasomotor innervation," and felt that it "ought to be considered as a neurosis characterized by enormous exaggeration of the excitomotor energy of the gray parts of the spinal cord which control the vasomotor innervation."[10] This conception was so well founded on clinical observation that its acceptance was universal. It was never questioned until the observations of Lewis[7] and Kerr led them to believe that the condition was due to a local fault which "displays itself in hypersensitivity of these vessels to relatively low temperatures." This hypothesis was so divergent from the generally accepted view that it caused renewed interest and experimental research into the fundamental characteristics of the disease. This resulted in the demonstration that, in some cases at least, the hypersensitivity of the vessels to cold was the primary fault. But those who challenged this view pointed out that in many cases the vascular spasm induced by cold was relieved by blocking the vasoconstrictor nerves. They contended that only in advanced cases of the condition was the local fault to cold effective. It was admitted that exposure of the extremity to cold would induce an attack, but it was felt that the cold was merely a stimulus which excites an overactive response of the vasoconstrictor nerves.

As evidence accumulates, it appears that both of these views are correct. The difference exists in the reaction of individual patients. Some have a vasomotor neurosis that is relieved by blocking the vasoconstrictor nerves. In others, sympathetic denervation has only a slight effect and will neither prevent nor relieve attacks of vascular spasm in the extremity subjected to appropriate degrees of cold. In both, whether it is primary or secondary, there is hypersensitivity to cold.

Emotional factors form another influence that calls forth an exaggerated response. In the normal person, emotion produces peripheral vascular changes. We speak of the "pallor of fear," the "blush of

*From the Department of Surgery, The University of Rochester, School of Medicine and Dentistry, Rochester, New York.

†Read before the American Heart Association, Atlantic City, June 11, 1935.

‡The term "Raynaud's disease" is used in its commonly accepted sense to denote a severe idiopathic vasospastic condition of the extremities. It may well be a symptom-complex rather than a disease entity.

embarrassment," or of an apprehensive person having "cold feet." Yet attacks of pallor, cyanosis, and pain do not occur in the extremities of normal persons as they do in patients with Raynaud's disease, in spite of the fact that the emotional stimulus may be the same in both. Nor does cold play a part here for these vasospastic attacks from psychic disturbance occur when the extremities are warm.

Recently Smithwick, Freeman, and White[13] have made the important observation that after sympathetic denervation the part becomes sensitized to epinephrine. They record the striking example of gangrene in such a sensitized extremity resulting from emotional disturbance. This was apparently due to excessive vasoconstriction induced by the patient's circulating adrenin.

There is evidence to support the view that the peripheral vessels in Raynaud's syndrome may be hypersensitive to cold, to vasomotor impulses, to emotion and, after sympathectomy, to epinephrine. This being true, it is possible that any normal stimulus may give an exaggerated vascular response. It leads to the conception that there is a local abnormality which causes an excessive reaction when normal stimulation is applied. If this were the case, then it is reasonable to suppose that body heat regulation would have influence, for this is one of the most important functions of the peripheral vasomotor mechanism. The skin of the extremities makes up about 65 per cent of the body surface. Its vessels are frequently constricting or dilating to perform the thermoregulatory functions of heat conservation or dissipation. With slight alteration of body temperature there is normally a wide fluctuation in that of the extremities.[3, 4] Consequently, if the peripheral vessels in Raynaud's disease are hypersensitive to normal stimuli, then alteration in body temperature should induce or relieve attacks of vascular spasm. The following experiments were designed to test this.

METHODS

Four typical patients with Raynaud's syndrome who had previously been studied by Morton and Scott[9] were readmitted. Two had severe cases of long standing. One of these had had loss of tissue from trophic changes. The majority of the studies were conducted with these cases. For the sake of comparison, the other two cases chosen were less severe, their attacks were not as painful nor as prolonged as in the severe cases and could be abolished by nerve block.

Observations were made in a constant temperature room at 19° to 21° C. Skin temperature readings were obtained with the dermatherm.[11]

The First Question.—If the hands are kept warm and the body cooled, will vascular spasm occur?

The hands may be warmed by covering them with blankets, a warm box, warm water, or electric pads, leaving the finger tips exposed for temperature readings. The body may be cooled by exposure to cold air as in an ice box, by a cold bath, or by drinking large amounts of ice water.

Experiment 1.—April 3, 1935. Subject F. B. S.M.H. 38360 (severe case). Room temperature 21.1° C.

The patient came to the constant temperature room from the division. The hands were slightly blue but not deeply cyanotic or painful. Preliminary temperature readings showed the digits to be 21° C. at 11 A.M.; the hands and forearms were placed in water at 42° C., the finger tips being exposed for temperature readings.

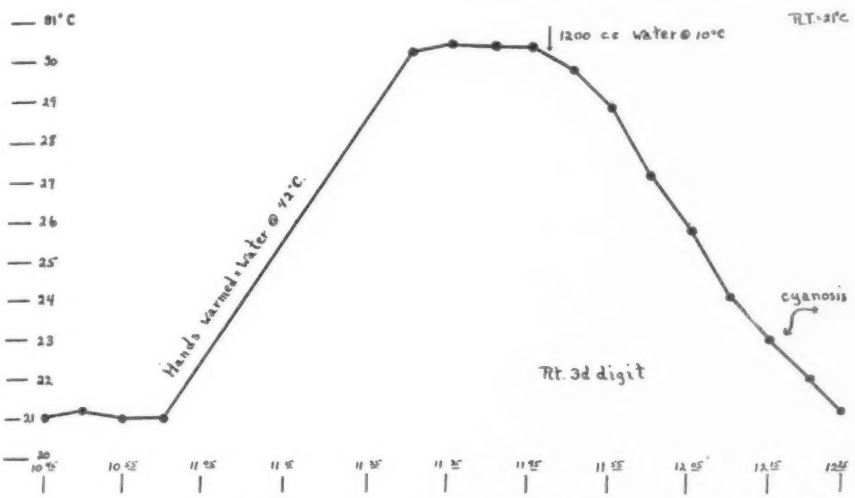

Fig. 1.—If the hands are kept warm, cooling the body causes vascular spasm in these extremities. The hands were warmed in water at 42° C. until they reached the vasodilatation level. The body was then cooled by drinking 1,200 c.c. of ice water. This caused a fall in the temperature of the finger tips and the onset of an attack of vasospasm with pain and cyanosis.

At 11:30 A.M. the temperature of the digits had risen to 30.2° C. The hands were pink; there was slight perspiration of the face; and the patient felt warm. At 11:45 he drank 1,200 c.c. of water at 10° C. This caused an immediate decline in the temperature of the fingers. At 12:05 he complained of feeling chilly. At 12:15 the hands became cyanotic. The temperature of the fingers was 23° C. Within ten minutes the temperature had fallen to 21° C. and there was vascular spasm with cyanosis and pain (Fig. 1).

I find one mention of a similar experiment. Simpson, Brown, and Adson[12] report their experience with two cases. In one, the patient, with hands wrapped in a blanket (temperature of fingers 33.4° C.), was left in an ice chamber at 2° C. for five minutes. In spite of the warmth of the hands, vascular spasm occurred. In another, the hands

were submerged in water at 38° C. and the patient was placed in the ice chamber for thirty minutes. Exactly the same result occurred.

It would appear that even with the hands warm, attacks of vasospasm may be induced by cooling the body.

The Second Question.—Will warming the body relieve vasospasm of the extremities?

This has already been answered in the affirmative by Lewis and Pickering.[8] They state that "it is clear that warming the body in Raynaud's disease will release digital arteries previously held constricted by cold." In their experiments a chamber heated with carbon arc lamps was used to warm the body. Other methods are the use

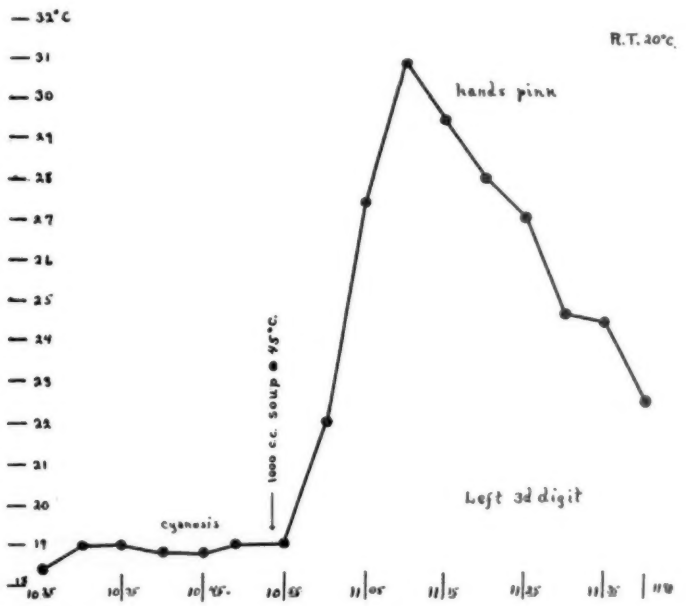

Fig. 2.—Warming the body will relieve an attack of vascular spasm even though the hands remain in a cool environment. In this experiment the subject's hands were very cyanotic and painful. She drank 1,000 c.c. of soup at 45° C. with resultant increase in temperature of the fingers and relief of the vasospasm. Other forms of warming the body, as by external heat, have the same effect.

of hot baths,[4] diathermy, wrapping the body in blankets,[3] or the drinking of hot liquids. That the latter will produce the effect is shown by the following experiment.

Jan. 10, 1935. Subject B. L. S.M.H. 19608. Room temperature 20° C.

The patient came to the examining room from out of doors. The hands were deeply cyanotic and painful. The temperature of the fingers was 18.4° C. She was observed from 10:25 until 10:55 A.M. without noticing any appreciable change in symptoms, appearance, or temperature. At this time she drank 1,000 c.c. of soup at 45° C. There was an immediate rise in the temperature of the fingers. In twenty minutes the temperature of the digits was 31° C. All evidence of vasospasm

disappeared, and the hands turned a normal pink color. The temperature of the digits soon fell, but symptoms did not return (Fig. 2).

The Third Question.—Can warming of the body prevent attacks of vasospasm if the hands are exposed to appropriate degrees of cold?

March 4, 1935. Subject C. D. S.M.H. 4638. Room temperature 21° C.

The patient came to the examining room from the division. The hands were cyanotic but not painful. The temperature of the fingers was 21° C. After preliminary observation for fifteen minutes the body was warmed by blankets and a rubber sheet.[3] Forty minutes later the digits were pink and warm, all spasm having been relieved. Their temperature had risen to 30.8° C. At 3:10 P.M. with the body kept warm the hands were submerged in water at 15° C. leaving the finger tips exposed. At 3:20 P.M. the temperature of the digits had fallen to 20° C..

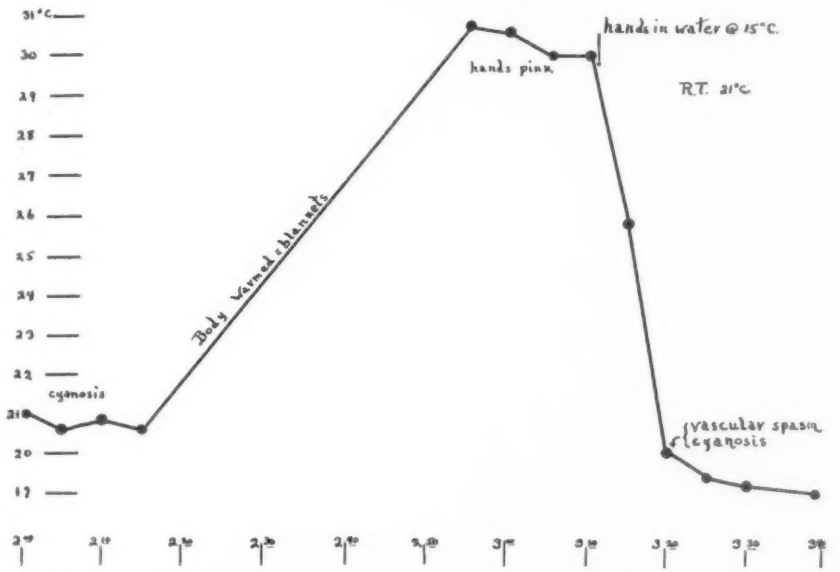

Fig. 3.—Keeping the body warm will not prevent an attack if the hands are subjected to appropriate degrees of cold. Here the subject's body was warmed in blankets until the hands reached the vasodilatation level. In spite of this, vascular spasm with pain and cyanosis occurred when the hands were placed in water at 15° C.

and vascular spasm with cyanosis and pain occurred. The experiment was discontinued at 3:40 because of the discomfort from the vasospasm (Fig. 3).

It is seen that warming the body did not prevent an attack of vascular spasm when the extremities were subjected to cold. This is in line with the conception that local exposure to cold forms the strongest stimulus to vasospasm in this condition.

The Fourth Question.—Is the heat derived from the digestion of food sufficient to prevent or relieve vasospasm?

It has been shown that the ingestion of food results in an increased blood flow.[5] Further, that during digestion there is an increase in both the body and skin temperature.[1] This has been confirmed.[6] The

"specific dynamic action" of the food increases body heat with consequent peripheral vascular dilatation to dissipate the surplus. It was reasoned that this effect might be utilized to prevent or abolish attacks of vasospasm in Raynaud's syndrome. If the "internal fires" were kept burning, there would always be a positive heat balance and hence little stimulus to vasoconstriction. Moreover, this would prevent hypoglycemia which has been shown[2] to stimulate the secretion of adrenin and so bring about vasospasm.[13]

The subjects were fed high protein meals containing 200 gm. of lean meat as well as high carbohydrate meals. Coffee or tea was not used, nor was the heat of the food sufficient to give an effect. There was no consistent alteration in the surface temperature of the digits at the time of eating nor for two hours after such meals. Attacks of vasospasm could be induced by exposure to cold and once instituted were not relieved by food. So it is seen that the test of this question gave negative results. But I am not at all satisfied with the findings. It is desirable that further study be done along this line, observing the subjects in a calorimeter rather than in a constant temperature room. In this way a more accurate check may be made upon their response to food. This is desirable, for, if the "specific dynamic action" of frequent feedings would diminish or prevent the attacks of vasospasm, it would be of some value in treatment.

SUMMARY

The influence of body heat regulation was observed in cases of Raynaud's disease. It was found that: (1) with the hands kept warm, cooling the body will cause an attack of vasospasm; (2) warming the body will relieve an attack; (3) warming the body will not prevent an attack if the hands are exposed to cold; and (4) the warming effect of food was inadequate to influence the vasospasm.

It is concluded that body heat regulation may have influence on the vasospasm of Raynaud's disease. This constitutes further evidence that normal forms of stimulation may give rise to an exaggerated vascular response. It suggests that a local abnormality causes this excessive spastic reaction from several diverse motivating factors.

REFERENCES

1. Burton, A. C., and Murlin, J. R.: Human Calorimetry: III. Temperature Distribution, Blood Flow and Heat Storage in the Body in Basal Condition and After Ingestion of Food, J. Nutrition **9**: 281, 1935.
2. Cannon, W. B., McIver, M. A., and Bliss, S. W.: A Sympathetic and Adrenal Mechanism for Mobilizing Sugar in Hypoglycemia, Am. J. Physiol. **69**: 46, 1924.
3. Coller, F. A., and Maddock, W. G.: The Differentiation of Spastic From Organic Peripheral Vascular Occlusion by the Skin-Temperature Response to High Environmental Temperature, Ann. Surg. **96**: 719, 1932.

4. Gibbon, J. H., Jr., and Landis, E. M.: Vasodilatation in the Lower Extremities in Response to Immersing the Forearms in Warm Water, J. Clin. Investigation **11**: 1019, 1932.
5. Herrick, J. F., Essex, H. E., Mann, F. C., and Baldes, E. J.: The Effect of Digestion on the Blood Flow in Certain Blood Vessels of the Dog, Am. J. Physiol. **108**: 621, 1934.
6. Herrick, J. F., and Sheard, C.: Changes in Surface and Rectal Temperatures in Man Produced by the Ingestion of Food Subsequent to Twenty-Four-Hour Fast. (To be published.)
7. Lewis, T., in collaboration with Kerr, W. J.: Experiments Relating to the Peripheral Mechanism Involved in Spasmodic Arrest of the Circulation in the Fingers, a Variety of Raynaud's Disease, Heart **15**: 7, 1929.
8. Lewis, T., and Pickering, G. W.: Vasodilatation in the Limbs in Response to Warming the Body; With Evidence for Sympathetic Vasodilator Nerves in Man, Heart **16**: 33, 1931.
9. Morton, J. J., and Scott, W. J. M.: Some Angiospastic Syndromes in the Extremities, Ann. Surg. **94**: 839, 1931.
10. Raynaud, M.: Quoted from Simpson, Brown and Adson.[12]
11. Scott, W. J. M.: An Improved Electrothermal Instrument for Measuring Surface Temperature, J. A. M. A. **94**: 1987, 1930.
12. Simpson, S. L., Brown, G. C., and Adson, A. W.: Raynaud's Disease, Arch. Neurol. & Psychiat. **26**: 687, 1931.
13. Smithwick, R. H., Freeman, N. E., and White, J. C.: Effect of Epinephrine on the Sympathectomized Human Extremity, Arch. Surg. **29**: 759, 1934.

THE EFFECT OF OUABAIN UPON THE ELECTROCARDIOGRAMS OF SPECIFIC MUSCLE LESIONS*

JANE SANDS ROBB, M.D., M. S. DOOLEY, M.D.,
J. G. FRED HISS, M.D., AND R. C. ROBB, M.D.
SYRACUSE, N. Y.

INTRODUCTION

THE effects upon the electrocardiogram caused by experimental ligation of the blood supply to a single ventricular muscle band in dogs have been described in a series of papers from this laboratory.[1-4] These same alterations have also been found to appear in electrocardiograms of monkeys (*Macacus rhesus*),[5] whose hearts are more similar to that of man.

If displacements of the R-T interval have a clinical application in localizing the site of a coronary obstruction and as a guide to treatment, then to know the effect of the digitalis group upon this interval is important.

In 1915, Cohn[6] observed that in man digitalis causes an inversion of the T-wave and also stated that, if the T-wave is initially negative, upon digitalization it again becomes positive. This action is not influenced by atropine and hence the seat of action is said to be in the muscle. Cushny[7] and Sollman[8] also describe vagal and direct muscular actions of digitalis.

EXPERIMENTAL PROCEDURE

Experiments have been devised to determine whether digitalis had an effect upon the R-T segment displacement which results from lesions in specified muscles.

Observations were made on six monkeys (*Macacus rhesus*) and five dogs. Because only acute experiments were feasible, ouabain was given intravenously. In some cases the animals were first given a therapeutic dose (0.05 mg. per kg.) and when its effects had developed (judged by flattening of T and prolongation of P-R), a muscle lesion was produced. In other experiments the lesion was produced first and the animal then given a toxic dose of ouabain (0.1 mg. per kg.). The operative procedure and other points of technic were the same as described previously.[1, 3] The hearts were removed at autopsy and subsequently dissected to establish the exact locations of the lesions.

*From the Departments of Pharmacology and Medicine, Syracuse University, Syracuse, N. Y., and from the Division of Pediatrics of the Strong Memorial Hospital, Rochester, N. Y.

RESULTS

Previous therapeutic dosage of ouabain did not prevent the appearance of the R-T change known to be characteristic of specific muscle lesions. Toxic dosage of digitalis did not affect the lesion electro-

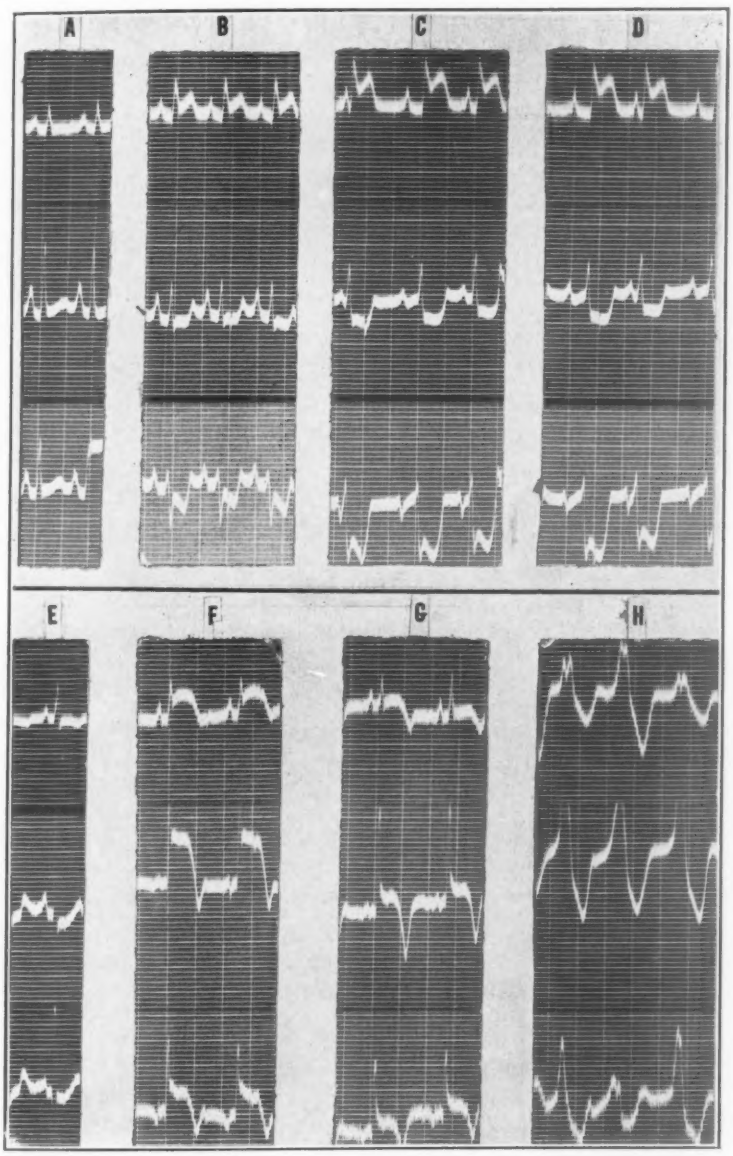

Fig. 1.—All tracings show simultaneous leads (I, II, and III from above downward). *A* is a control record; *B*, following a lesion of the DSS muscle; *C* and *D* show this characteristic alteration to be exaggerated by therapeutic and toxic amounts of ouabain, respectively.

E is a control record; *F*, following a lesion of the DBS; while *G* and *H* show the tendency of therapeutic and toxic doses of ouabain to remove the effect characteristic of the muscle lesion.

cardiograms of different muscles in the same manner, hence one must present data and discuss each muscle separately.

In Table I are summarized the changes in T and R-T under therapeutic and toxic dosage of ouabain for comparison with the changes in the untreated muscle lesion.

TABLE I

MUSCLE	R-BASE INEQUALITY EXPRESSED IN 0.1 MV.			R-BASE INEQUALITY EXPRESSED IN 0.1 MV.		
	MUSCLE LESION			MUSCLE LESION PLUS OUABAIN		
	LEAD I	LEAD II	LEAD III	LEAD I	LEAD II	LEAD III
SSS	+1.0	+1.3	+1.0	+0.3	+0.25	±0.0
SBS	−1.0	+2.0	+1.5	−0.3	+1.5	+1.1
DSS	+1.5	−1.5	−2.5	+1.0	−2.75	−5.0
DBS	+3.0	+5.25	+2.5	+0.5	+1.5	+1.1

In the case of the superficial muscles, ouabain in therapeutic amounts has little effect either on the T or R-T. In toxic doses the R-T shifting in all leads is reduced.

When a *deeper* muscle is anemic, the effects of ouabain are far more pronounced. If the drug is given in therapeutic amounts before ligation of the branches from the left circumflex to the deep bulbospiral, the marked elevation of R-T still occurs but this is followed by a very negative T, whereas in the untreated condition the T is wholly positive (Fig. 1 *F*). If the ouabain concentration is increased to toxic amounts, the R-T shoulder drops toward the isoelectric level, and the T becomes progressively more negative until the heart stops.

Lesions in the deep sinospiral muscle in the presence of ouabain produce quite a different electrocardiographic picture (Fig. 1 *A* to *D*). Therapeutic dosage leaves the elevation of R-T in Lead I relatively unaltered but markedly augments the already existing depression in Leads II and III. As toxicity intervenes, the elevation in Lead I and the depression in Leads II and III are still further exaggerated until just before death, when the voltage suddenly decreases.

All of these tracings have been read with a Cambridge measuring instrument. In Table II are presented average results along with control data. (a) As would be expected, the muscle lesions had no effect upon the P-R interval, for the vessels ligated were definitely

TABLE II

	P-Q	QRS	QT	ST	RATE
Dogs—pentobarbital 50 mg./kg.	0.098	0.041	0.229	0.175	168
Monkeys—pentobarbital 50 mg./kg.	0.069	0.027	0.245	0.216	161
Dogs—pentobarbital + muscle lesion	0.091	0.039	0.237	0.189	141
Monkeys—pentobarbital + muscle lesion	0.087	0.032	0.361	0.300	113
Dogs—pentobarbital + muscle lesion + ouabain	0.128	0.042	0.290	0.236	80
Monkeys—pentobarbital + muscle lesion + ouabain	0.170	0.058	0.404	0.322	35

chosen so that the blood supply to the conduction system would be unaffected. The P-R interval is lengthened by ouabain. (b) The QRS also is uninfluenced by the muscle lesions, but, as toxicity under ouabain appears, the interval becomes greater. These data would support the opinion that the muscle lesions do not interfere with the spread of excitation as indicated by the duration of QRS. (c) The Q-T and S-T are increased by the muscle lesions and still more by the ouabain. This fact, together with the observed effects upon the R-T and T phases, seems to indicate that the effect of the lesions is upon portions of the contractile mechanism without involving the chief conducting pathways. This increase in Q-T and S-T cannot be relieved by vagal section, nor are the displacements of R-T altered either during vagal stimulation or after vagal section. Three observations, then, support the supposition that the changes in the electrocardiogram consequent to anemic infarcts are produced by injuries to muscular rather than to nervous structures: (1) These changes occur if the vagi are cut and are uninfluenced during vagal stimulation; (2) these characteristic changes are influenced by ouabain in that part of the electrocardiogram where ouabain has been stated to exert its effect by direct action on the muscle; (3) the S-T and Q-T are prolonged by these infarcts whereas the QRS is not.

It is not considered that there are data either in the literature or in these experiments which would differentiate between an action upon muscle fibers or upon the peripheral ramifications of the Purkinje material within the muscle bands.

SUMMARY AND CONCLUSIONS

1. Anemic infarcts localized to one ventricular muscle band have been produced experimentally in dogs and monkeys.

2. The electrocardiographic change produced is characteristic for each muscle.

3. Ouabain in therapeutic doses does not prevent the appearance of these characteristic changes in the electrocardiogram.

4. Ouabain in toxic doses tends to diminish the electrocardiographic change characteristic for three muscles, namely, the superficial bulbo- and sinospiral, and the deep bulbospiral muscle.

5. Ouabain in therapeutic and toxic doses tends to increase the electrocardiographic change found to be characteristic for the deep sinospiral muscle.

6. Neither the R-T or T changes due to the muscle lesions nor those due to the ouabain are influenced by vagal section.

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REFERENCES

1. Robb, Jane Sands: Evidence for Characteristic Modifications of the Electrocardiogram Produced by Lesions of Ventricular Muscle Bands, Proc. Exper. Biol. & Med. 31: 311, 1933.
2. Robb, Jane Sands: Progressive Muscular Anemia in the Heart of a Dog, Proc. Exper. Biol. & Med. 31: 761, 1934.
3. Robb, Jane Sands; Easby, Mary; and Hiss, J. G. F.: Experimental Interference With Conduction in the Heart, Am. J. M. Sc. 188: 835, 1934.
4. Robb, Jane Sands; Hiss, J. G. F.; and Robb, R. C.: Localization of Cardiac Infarcts According to Component Ventricular Muscles, AM. HEART J. 10: 287, 1935.
5. Robb, Jane Sands, and Robb, R. C.: Coronary Ligation in Monkeys, in press, 1935.
6. Cohn, Alfred E.: Influence of Digitalis on the T-Wave of the Human Electrocardiogram, J. Exper. Med. 21: 593, 1915.
7. Cushny, A. R.: Pharmacology and Therapeutics, ed. 10, revised by C. W. Edmunds and A. J. Gunn, Philadelphia, 1934, Lea & Febiger, pp. 480, 481.
8. Sollman, Torald: Manual of Pharmacology, Philadelphia, 1932, W. B. Saunders Company, pp. 517-522.

THE RESULTS OF TREATMENT IN CARDIOVASCULAR SYPHILIS*

A Report of Three Years' Additional Observation

Paul Padget, M.D.,† and Joseph Earle Moore, M.D.
Baltimore, Md.

In 1930 one of us (J. E. M.) with Danglade[1] presented to this association a preliminary report on the treatment of cardiovascular syphilis, based upon a study of 141 patients. The conclusions reached were later amplified and extended in a detailed analysis of 165 cases published with Danglade and Reisinger[2] in 1932. The preliminary report included eight cases in which the diagnoses might be questioned; the later study was purposely limited to patients with saccular aortic aneurysm or syphilitic aortic insufficiency.

When this study was completed on July 1, 1931, an effort had been made to trace each of the patients, numbering a few over 300, with definite diagnoses of saccular aortic aneurysm or syphilitic aortic insufficiency, whose names were in the files of the Syphilis Division, and the 165 reported included all whose status could be determined as of that date.

In evaluating the usefulness of specific therapy in these conditions, the patients were divided into four groups on the basis of the amount of treatment they had received; and it was shown, we thought, that properly directed antisyphilitic treatment resulted in alleviation of symptoms and prolongation of life, with consequent reduction in mortality rate for an incomplete period of observation.

Many remained unconvinced, however, and Barnett,[3] in criticizing the method of study employed and in reporting his own experience, concluded that there was no evidence to indicate that antisyphilitic treatment is beneficial to patients with aortic insufficiency or aneurysm. It seemed wise, therefore, to reexamine the subject.

The present study deals with the same group of patients previously reported.[2] On July 1, 1931, 109 of the 165 discussed were dead. Four of the fifty-six who remained alive could not be traced; the remainder have been followed up to Jan. 1, 1935, thus forming a group of 161 patients in which the mean potential period of observation has been ten years and eight months, with a minimum period of observation of any living patient of five and a half years. No effort was made

*From the Syphilis Division of the Medical Clinic, Johns Hopkins Hospital.
†Eli Lilly research fellow in medicine.
Read before the American Heart Association, Atlantic City, N. J., June 11, 1935.

to add additional cases; it was thought that the long period of observation available in this group was the most valuable feature of the study.

The data which bear on the evaluation of antisyphilitic treatment have been entirely recalculated and several changes in the method of analysis have been made. Duration of life is expressed as mean instead of as average, in order to facilitate the determination of the statistical significance of differences. The information concerning causes of death has been again reviewed, and the deaths divided into those directly due to cardiovascular syphilis, and those due to other diseases, or due to unknown causes.

A simpler division into two treatment groups has been substituted for the four groups of the former report. In an "inadequate treatment" group have been placed those patients who received the equivalent of one course of an arsenical, or a long course of heavy metal, or less; while the "adequate treatment" group includes those who received a course of an arsenical plus heavy metal, two long courses of heavy metal, or more. Such a division is arbitrary and the minimum of the latter group may not truly be said to constitute adequate antisyphilitic therapy. Fortunately in this series, however, there was little gradation about the dividing line; the majority had received either very small or relatively large amounts of treatment.

The most important change in the method of analysis was suggested by Barnett's[3] well-taken exception to the propriety of including in the "inadequate treatment" group those patients who, because of an originally bad prognosis, died so soon that adequate treatment could not have been given. Accordingly, and as a result of studies to be elaborated elsewhere,[4] which show that those dying quickly should be considered as a separate group, the fifty-three patients (33 per cent of fhe total) who died within less than a year after they came under observation have been removed from a consideration of therapeutic results.

As in the previous paper, duration of life has been calculated from the onset of symptoms referable to the cardiovascular system, or to the establishment of a definite diagnosis in the few instances in which symptoms were indefinite. This obviously introduces some uncertainties, but no more applicable method has been suggested.

An effort had been made to give to every patient adequate antisyphilitic treatment; excluding those who died quickly, patients were inadequately treated only because of lack of cooperation. In this regard Barnett[3] has suggested that patients who are so uncooperative that they fail to return for treatment also do not follow instructions in regard to limitation of activity and general medical care, and that

therefore untoward results in such a group should be charged to lack of therapy in general, rather than to lack of antisyphilitic treatment. The individual variation in ability to understand and willingness to follow instructions is so great as to prohibit generalizations of this sort, and careful study[4] has convinced us that our "inadequate treatment" and "adequate treatment" groups vary in no way from each other, as to the apparent severity of their illness or the kind and extent of general medical care, except only in the amount of antisyphilitic treatment received.

Table I shows that the 161 patients are almost equally divided into three groups. One-third of them died within less than a year of observation, and with few exceptions received no antisyphilitic treatment, mainly because the onset and progress of their fatal illness was so abrupt as to exclude its possibility. Another third survived for more than one year but received inadequate treatment. The remaining one-third fell into the "adequate treatment" group. Fifteen (29 per cent) of the 52 patients with aneurysm and 38 (35 per cent) of the 109 with aortic insufficiency died within the first year of observation; 17 (33 per cent) of those with aneurysm and 36 (33 per cent) of those with aortic insufficiency received inadequate treatment; while 20 (38 per cent) of the patients with aneurysm, and 35 (32 per cent) of those with aortic insufficiency, were adequately treated. The distribution of cases is therefore quite symmetrical.

TABLE I

THE DISTRIBUTION INTO GROUPS OF 161 CASES OF CARDIOVASCULAR SYPHILIS

	NUMBER OF CASES	NUMBER PATIENTS DEAD	ANEURYSM		AORTIC INSUFFICIENCY	
			NUMBER OF CASES	NUMBER DEAD	NUMBER OF CASES	NUMBER DEAD
Total	161	123	52	41	109	82
Died in less than one year	53	53	15	15	38	38
Total, inadequate treatment and adequate treatment	108	70	37	26	71	44
Inadequate treatment	53	46	17	14	36	32
Adequate treatment	55	24	20	12	35	12

Of the 108 patients available for a consideration of the results of treatment, 53 (49 per cent) received inadequate treatment, and 55 (51 per cent) were adequately treated. The "inadequate treatment" group includes 17 individuals with aneurysm and 36 with aortic regurgitation; the "adequate treatment" group comprises 20 with aneurysm and 35 with aortic insufficiency.

This study may be considered complete only when all of the patients are dead, but in the meantime a comparison of the mortality

rates of the two groups affords valuable information. Figure 1 presents such comparison. Fourteen (82 per cent) of the 17 patients with aortic aneurysm who received inadequate treatment are dead; and in eleven of these (65 per cent) death was due to the cardiovascular disease. In contrast, 20 patients with aneurysm were adequately treated; 12 (60 per cent) of these are dead, but only 8 (40 per cent) died from cardiovascular syphilis. In those patients with aortic insufficiency, the reduction in mortality due to cardiovascular syphilis is even more striking. The numbers receiving inadequate and adequate treatment are almost exactly equal. Thirty-six were inadequately treated, and 35 received adequate treatment. Thirty-two (89 per cent) of the former are dead, twenty-three of them (64 per

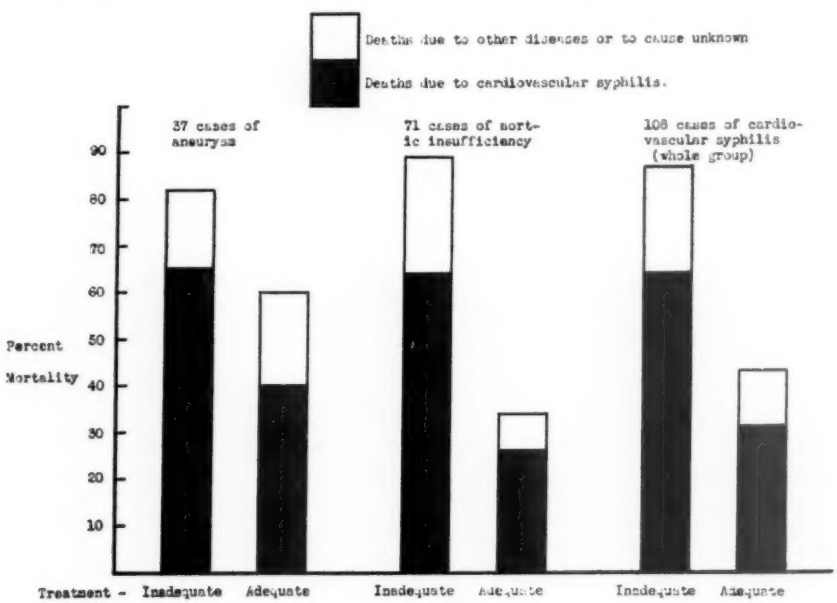

Fig. 1.—The mortality rate of 108 patients with cardiovascular syphilis observed for more than one year in reference to the amount of antisyphilitic treatment received.

cent) from heart disease; while only 12 (34 per cent) of the latter have died, and only 9 (26 per cent) of these from cardiovascular syphilis.

Considering the group as a whole, 46 (87 per cent) of the 53 inadequately treated patients are dead, while only 24 (43 per cent) of the 55 well-treated have succumbed, while deaths known to be due to cardiovascular disease are 34 (64 per cent) in the former, and 17 (31 per cent) in the latter.

Figure 2 contrasts the duration of life from the onset of symptoms to death in the seventy treated patients who have died. Of the patients with aneurysm the fourteen dead who were inadequately treated

lived a mean of thirty-two months after developing symptoms, while the twelve who had received adequate treatment lived fifty-five months. In those with aortic insufficiency the 32 dead who had been inadequately treated lived a mean of forty-five months, and the twelve dead in the "adequate treatment" group lived sixty-one months.

Again considering the group as a whole, the 46 inadequately treated patients survived for a mean of forty-one months after the development of symptoms, while the 24 who received adequate treatment lived for sixty months.

In a later communication[4] we shall demonstrate in detail that the differences between the two treatment groups are statistically signi-

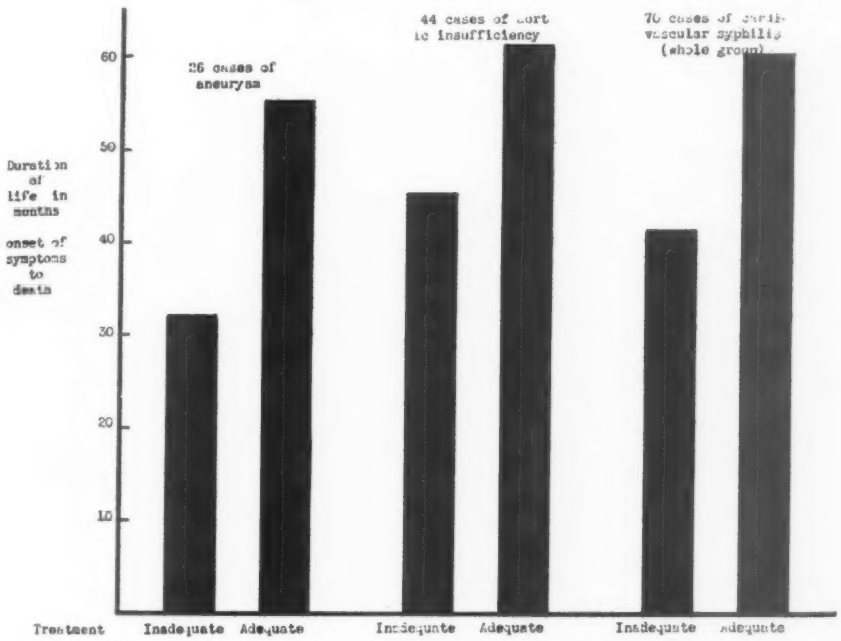

Fig. 2.—The duration of life in seventy dead patients who had cardiovascular syphilis and were observed for more than one year in reference to the amount of treatment.

ficant, with the exception of the difference in duration of life between adequately and inadequately treated patients with aortic insufficiency. There the number dead who were adequately treated was so small and the durations observed in the individual cases were so variable that from the statistical standpoint a large probable error is introduced.

The full significance of these figures may be appreciated only by comparing the observed duration of life in those dead with the mortality rates of the two groups. The surviving patients in both groups have lived on the average approximately ten years, i.e., far in excess of the duration of life in those already dead. However, only 7 of the

53 patients inadequately treated survive, while 31 of the 55 adequately treated are still alive. It is readily apparent that when all of the patients are dead, the duration of life in the well-treated group will be vastly in excess of the survival period of those poorly treated.

Confirmation of our proof as to the value of treatment in cardiovascular syphilis has been provided by Grant.[5] In the course of his monumental study of the clinical course of a thousand patients with heart disease, 189 patients with syphilitic aortic insufficiency were followed either to death or for a minimum observation period of ten years. Part of these had been allowed to go without antisyphilitic therapy, a larger group had been given potassium iodide, and the remainder had received potassium iodide and neoarsphenamine in

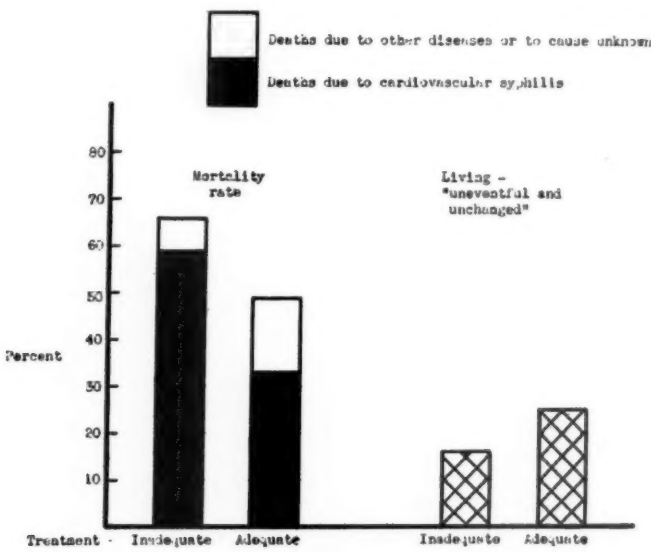

Fig. 3.—The outcome in 171 patients with syphilitic aortic insufficiency (after Grant).

varying amounts, with interval mercury by inunction. The general medical care was the same for all groups.

We have analyzed the very complete data given by Grant for each case by the same methods employed for our own. Eighteen of the cases were deleted because of inadequate information. Of the 171 remaining, 51 had received at least one course of six injections of neoarsphenamine, mercury by inunction, and potassium iodide by mouth; 75 had received potassium iodide by mouth only; and 45 had been given no antisyphilitic treatment. Grant's study and our reanalysis revealed no significant differences between these last two groups, which have therefore been consolidated to form an "inadequate treatment" group, while the former was considered as an "adequate treatment" group.

Figure 3 contrasts the mortality rate and the number living, in Grant's words, "uneventful and unchanged," in the two groups. Twenty-five (49 per cent) of the 51 patients who received specific therapy were dead at the end of ten years; in 17 (33 per cent) death was due directly to cardiovascular syphilis. Of the 120 patients in the "inadequate treatment" group, 79 (66 per cent) died during the same period; 71 (59 per cent) from cardiac disease. In contrast to this, 13 (25 per cent) of the adequately treated, but only 19 (16 per cent) of the inadequately treated, had survived the ten-year period to be adjudged "uneventful and unchanged." There was no significant difference in the duration of life between the well- and poorly treated groups.

SUMMARY

1. An analysis of the course of 161 patients with outspoken forms of cardiovascular syphilis is presented with reference to the effect of antisyphilitic treatment. Fifty-two of the patients had saccular aortic aneurysm; 109 had syphilitic aortic insufficiency.

2. One-third (53) of the patients died in less than a year of observation, and these are considered in a separate group, as unamenable to the beneficial effects of specific therapy because of the gravity of their disease and its rapid progress.

3. One hundred and eight survived for more than a year of observation and received varying amounts of antisyphilitic treatment. Of these, 53 are considered in an "inadequate treatment" group and 55 in an "adequate treatment" group.

4. The mean potential period of observation was ten years and eight months.

5. The mortality rate for the poorly treated group was 1.37 times that of the well-treated group in patients with aneurysm; 2.62 times as great in those with aortic insufficiency; and 2.02 times as great for the group as a whole.

6. The deaths due to cardiovascular syphilis were 1.62 times as great in the poorly treated as in the well-treated patients with aneurysm; 2.46 times as great in those with aortic insufficiency; and 2.06 times as great for the whole group.

7. Seventy patients of the series are dead.

8. The duration of life from onset of symptoms for those dead was 1.47 times as great in the well-treated as in the poorly treated patients for the whole group; 1.71 times as great in those with aneurysm; and 1.37 times as great in the patients with aortic insufficiency. The latter figure is not of certain statistical significance.

9. A restudy of Grant's cases of syphilitic aortic insufficiency was made.

10. The mortality rate of his poorly treated group was 1.35 times that of those well treated; deaths due to cardiac disease were 1.78 times as frequent in the former as in the latter.

11. No significant difference in the duration of life in his two groups was observed.

CONCLUSIONS

Properly directed antisyphilitic therapy results in a prolongation of life in two-thirds of the patients with saccular aortic aneurysm or syphilitic aortic insufficiency. The remaining third come under observation with an initially bad prognosis and do not survive sufficiently long for proper therapy to be administered.

REFERENCES

1. Moore, J. E., and Danglade, J. H.: The Treatment of Cardiovascular Syphilis, AM. HEART J. 6: 148, 1930.
2. Moore, J. E., Danglade, J. H., and Reisinger, J. C.: Treatment of Cardiovascular Syphilis, Arch. Int. Med. 49: 879, 1932.
3. Barnett, C. W.: Effect of Specific Treatment on the Prognosis of Syphilis of the Cardiovascular System, Arch. Dermat. & Syph. 28: 1, 1933.
4. Padget, Paul, and Moore, J. E.: The Treatment of Cardiovascular Syphilis. (In press.)
5. Grant, R. T.: After-Histories for Ten Years of a Thousand Men Suffering From Heart Disease, Heart 16: 275, 1933.

THE FORM OF THE ELECTROCARDIOGRAM IN EXPERIMENTAL MYOCARDIAL INFARCTION

IV. Additional Observations on the Later Effects Produced by Ligation of the Anterior Descending Branch of the Left Coronary Artery* †

Frank N. Wilson, M.D., Franklin D. Johnston, M. D., and Ian G. W. Hill,‡ M.B.
Ann Arbor, Mich.

IN PREVIOUS articles of this series we have had occasion to refer to certain pecularities in the form of the RS-T segment and T deflection observed in direct leads from the peripheral portions of subacute infarcts induced by ligation of the anterior descending branch of the left coronary artery. We have mentioned the characteristic modifications of the QRS deflections frequently seen in the same leads and also in leads from regions where only the inner layers of the ventricular wall are infarcted. Finally, we have commented upon the resemblance between the ventricular complexes inscribed in leads from infarcted portions of the ventricular wall which are no longer responding to the excitatory process and those obtained by introducing the exploring electrode into the cavity of the left ventricle. It is our present purpose to describe experiments in which more extensive observations relating to these phenomena were carried out, and to discuss their significance.

The methods employed in our experiments have been fully described in previous articles.[1, 2, 3] We may again point out that all direct and semidirect leads were taken simultaneously with standard Lead I and with a vacuum tube in the galvanometer circuit. The exploring electrode was paired with an electrode of the same type placed in contact with the subcutaneous tissues of the left (occasionally of the right) hind leg.

For the purpose of determining whether the subepicardial muscle in a given region was living or dead, we made extensive use of a sharp electrode, which consisted of a short length of enameled copper wire sharpened at one end, where the insulation was scraped off for a distance of one or two millimeters. The form of the ventricular complexes obtained when such an electrode is pressed against the surface of the heart has been described elsewhere.[5] When the subepicardial muscle is dead, the curve obtained is identical with that recorded by means of

*For previous articles of this series see Wilson, Hill, and Johnston,[1, 2] and Johnston, Hill, and Wilson[3]. The observations reported in this article were briefly described in a paper read at a recent meeting of the Association of American Physicians[4].

†From the Department of Internal Medicine, University of Michigan Medical School.

‡Of the Department of Medicine, University of Aberdeen.

a soft-tipped electrode of the ordinary type. In the article referred to, it was pointed out that, when this muscle is normal, a reduction in the height of the intrinsic deflection and pronounced downward displacement of the RS-T segment results, but the form of the preintrinsic portion of the ventricular complex is not altered. This principle is illustrated exceptionally well by the curves of Figs. 5 and 6 of this article.

ILLUSTRATIVE EXPERIMENTS

Experiment I (Dog 44).—In this instance the electrocardiographic observations were begun about twelve hours after ligation of two large subdivisions of the anterior descending branch of the left coronary

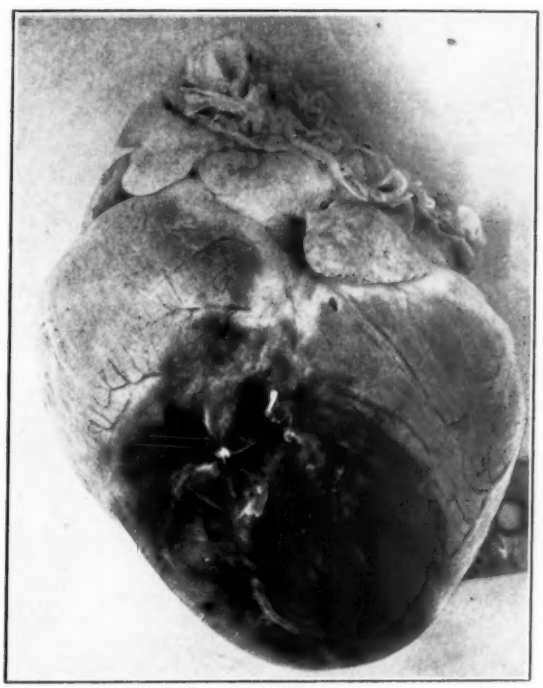

Fig. 1—Experiment I (Dog 44). Photograph of the left anterolateral surface of the heart showing the location and extent of the infarcted region.

artery. The chest had been carefully restored immediately after the ligation operation, and, before it was again opened, the standard leads and a set of three precordial leads were taken. The standard curves showed conspicuous upward displacement of the RS-T segment in Leads II and III and slight upward displacement of this segment in Lead I. Distinct, but not abnormally large, Q deflections were present in all three leads. The precordial leads were taken by pairing a copper disk (about one inch in diameter and fitted with a suitable binding post) sewn beneath the skin with an indifferent electrode on the right hind leg. Three such disks were arranged along a line which made an angle

of about 40 degrees with the long axis of the body. The first was placed in the midline and yielded a curve in which the QRS group began with a small downward movement. The second was placed 6 cm. and the third 12.5 cm. to the left of the midline. Both yielded curves in which the first and most prominent deflection of the QRS group was upward. The T deflection was sharply inverted in all three curves.

When the heart was exposed, the infarct appeared as a large hemorrhagic area on its left anterolateral margin. This area was roughly elliptical; its greater diameter measured about 5 cm. and its smaller diameter about 4 cm. (Fig. 1). At the end of the experiment the heart was sectioned, and it was found that, in the central portions of the region affected, the infarct extended completely through the ventricular wall. Near the margins of this region the involvement was patchy. On

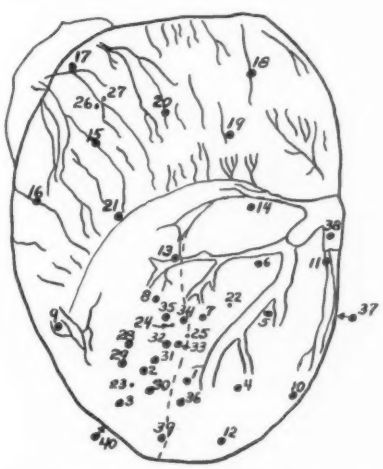

Fig. 2.—Experiment I (Dog 44). Outline drawing of the anterior surface of the heart showing the location of the points from which direct leads were taken. The broken line marks approximately the right border of the infarct.

the endocardial surface the limits of the infarct were rather poorly defined, but the area involved appeared to be approximately as large as on the outer surface.

The points from which direct leads were taken are indicated on an outline drawing of the anterior surface of the heart shown in Fig. 2, and samples of the curves obtained are reproduced in Fig. 3. The curves from points *9, 15, 16, 17, 18, 19, 20, 21,* and *40,* all outside the boundaries of the infarcted region, are of the type usually obtained from corresponding points on the surface of the undamaged heart.[5] The QRS group begins with a conspicuous downward movement, which is immediately followed by the intrinsic deflection, a sharp upstroke of large amplitude represented by a thin, barely visible line. A sharp exploring electrode pressed against the ventricular wall at point *26* yielded a curve in which QRS and T are completely fused. The descending

limb of this monophasic curve is interrupted by a notch which marks the position of the intrinsic deflection abolished by the injury. A curve obtained from the cavity of the right ventricle at point *27* shows a small preliminary downward movement followed by a tall summit; the RS-T segment and T are represented by a deep U-shaped depression.

The curves from the central portion of the infarcted region (points *4, 5, 6, 10, 11, 12,* and *37*) are similar to those obtained from the infarcted region in the experiments described in the third article[2] of this series. The ventricular complex is essentially diphasic and consists of a tall initial summit followed by a rounded depression, which, in some instances, ends with a small elevation above the base line. In the curves from points *5, 10, 11,* and *12* the initial summit is the sole deflection of the QRS group, and there is no trace of a true intrinsic upstroke. Curves of almost identical contour were obtained by thrusting a sharp electrode first into the wall and later into the cavity of the left ventricle at point *22.* We may conclude that at these points the ventricular wall was dead and was not responding to the excitatory process.

In the curve from point *4* the descending limb of the chief deflection dips below the base line, and there is an upward movement about one millimeter before the gradual slope of the RS-T segment begins. In the curve from point *6,* which is similar, the amplitude of the upward movement varies rhythmically between 0.5 cm. and 9 mm. Similar variations in the form of the ventricular complex are seen in the curves from several points. They are apparently due to slight to-and-fro movements of the exploring electrode caused by rhythmic inflation of the lungs. In the curves from points *37* and *38* there is a small but sharp upstroke which produces a conspicuous notch on the descending limb of the rather low initial summit. It is probable that these upstrokes represent intrinsic deflections of very small amplitude.[2]

The curves from the other points investigated, which were on or near the marginal portions of the infarcted region, are more difficult to describe. They vary greatly in form, and many of them show rhythmic variations of the kind already mentioned in the shape of the ventricular complex. As a class, these curves are characterized by the presence of both an abnormally tall initial summit and a conspicuous intrinsic upstroke. Many of them also display final deflections of unusual contour.

The curves from points *13* and *34* and some of the complexes of the curve from point *39,* however, are exceptions to this rule. The QRS group consists of a single tall upward deflection, and the intrinsic upstroke, if it is present, cannot be identified. In the first of these curves T is inverted; in the third it is sharply upright and of large amplitude; in the second a depressed RS-T segment is followed by a sharp upstroke which rises well above the zero level.

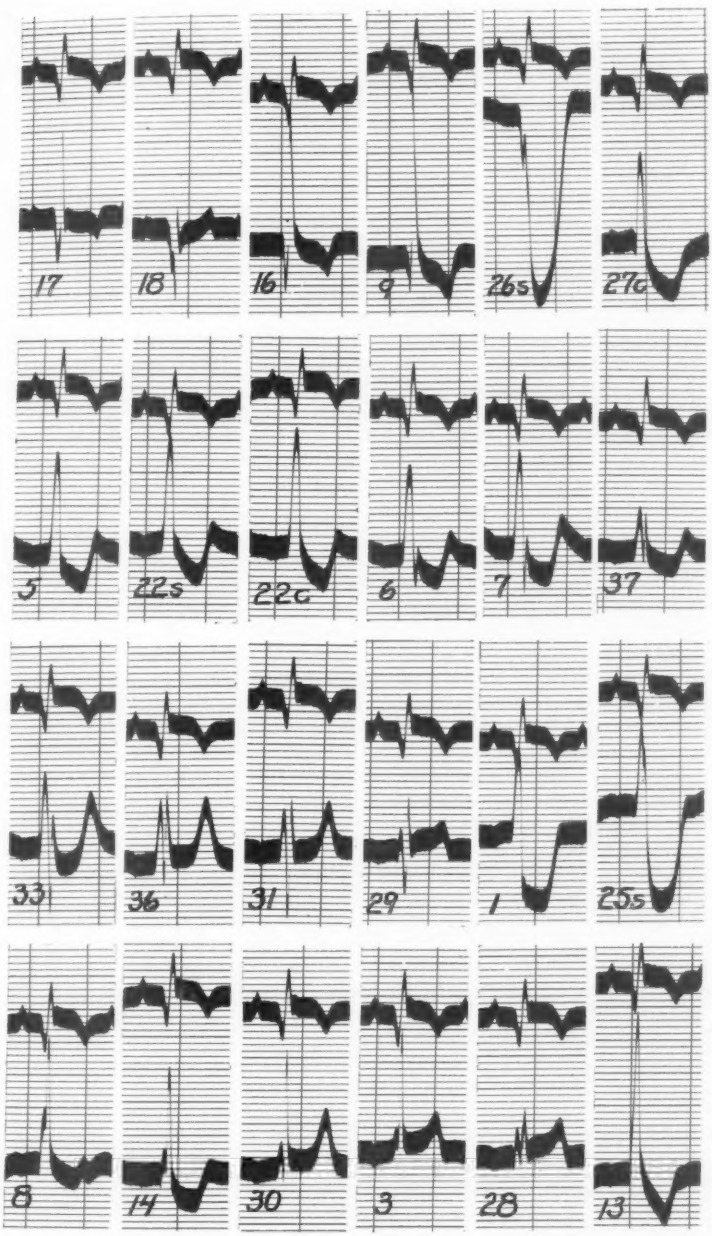

Fig. 3.—Experiment I (Dog 44). Direct leads from the points marked with corresponding numbers in Fig. 2. The letter *s* indicates that a sharp electrode was used and was pressed againt the epicardial surface. The letter *c* indicates that the sharp electrode was pushed through the ventricular wall into the ventricular cavity. The upper curve in all records is standard Lead I. In taking direct leads, the connections were so made that relative negativity of the exploring electrode is represented by an upward deflection, and the galvanometer was adjusted to give a deflection of 1 cm. for a potential difference of 20 mv.

The remaining curves differ chiefly in respect to the height of the initial summit, to the amplitude of the intrinsic upstroke, to the magnitude of the downward movement that separates these two deflections, and to the character of the RS-T segment and T deflection. The curves from points *2, 7, 31, 32, 33* and *36* are very much alike and have a very characteristic outline. The upward movement at the beginning of the QRS interval is large, but the downward excursion which follows it is larger and in most instances carries the string shadow well below the base line. The downward movement ends with the onset of the intrinsic upstroke, which is represented by a very thin line and is of moderate amplitude. The RS-T segment is flat or depressed and T is sharply upright and in most instances exceptionally tall.

In the curve from point *1,* which is close to and between points *33* and *36* and might be expected to yield a similar curve, the tall initial summit and the large downward movement are present, but there is no intrinsic upstroke and the RS-T segment is displaced downward nearly a centimeter. The peculiarities of this curve are undoubtedly due to injury effects induced by pressing the exploring electrode too firmly against the heart. A curve of strikingly similar outline was obtained at point *25* (very close to point *33*) by thrusting a sharp electrode into the superficial layers of muscle.

In the curves from points *29* and *30* the initial upward movement is no larger than that sometimes seen in normal epicardial curves, and, although the curve from the former point resembles the curves under consideration in general outline, it cannot be considered definitely abnormal. The curve from the latter point shows rhythmic variations in form which affect the depth of the downward movement and the shape and height of T. In some complexes the downward movement crosses the base line, and T is very tall and is preceded by a flat RS-T segment; in others it fails to cross the base line, and T has a more normal shape. The curve obtained by pressing a sharp electrode against the muscle at point *23,* which is between points *29* and *30,* is similar to that obtained in the same way at point *25,* but the upward movement is smaller and in some complexes is preceded by a small excursion downward. A mere trace of a similar initial downward movement is visible in some of the complexes of the curve from point *29.*

In the curve from point *28* the initial upward movement is small. The downward excursion which follows it barely crosses the base line, and the succeeding upstroke is slow and of small amplitude. The T deflection shows rhythmic variations in form; in some complexes it is unusually tall but not peculiar in other respects.

The curves from points *8* and *35* are characterized by the smallness of the downward movement which separates the initial summit and the onset of the intrinsic upstroke. In many of the complexes this downward movement is absent, and the junction of the initial summit and

TABLE I

MEASUREMENTS OF THE CURVES OF EXPERIMENT I (DOG 44)*

POINT	VOLTAGE OF INITIAL SUMMIT	LEVEL OF INTRINSIC ONSET	TIME OF INTRINSIC ONSET	AMPLITUDE INTRINSIC DEFLECTION	RANGE OF FINAL DEFLECTION	
9	–	9.6	0.010	60.0	11.6	0.0
15a	–	8.0	0.020	41.6	8.0	– 4.0
15b	–	4.0	0.015	32.2	10.0	– 1.6
16	–	10.0	0.008	42.0	6.4	0.0
17a	–	4.0	0.022	31.6	4.0	0.0
17b	–	6.0	0.025	26.0	2.8	0.0
18a	–	22.0	0.031	27.4	2.0	– 4.6
18b	–	31.6	0.034	41.0	3.0	– 5.4
19a	–	7.0	0.027	9.6	15.6	– 1.8
19b	–	12.4	0.023	45.4	6.0	– 6.2
20a	–	13.4	0.022	25.6	9.2	0.0
20b	–	8.0	0.018	25.0	10.6	0.0
21	–	4.0	0.009	53.6	12.6	0.0
40	–	19.0	0.019	47.2	0.0	– 4.0
5	–28.0	–	–	–	8.6	– 4.1
10	–21.8	–	–	–	14.0	– 2.0
11	–12.0	–	–	–	6.0	– 3.0
12a	–21.6	–	–	–	11.0	– 1.6
12b	–30.0	–	–	–	16.0	0.0
4	–28.0	8.3	0.048	3.4	12.0	– 2.0
6a	–24.0	4.8	0.037	2.8	7.2	– 4.2
6b	–24.0	10.0	0.042	17.4	6.0	– 4.8
37a	–10.8	2.0	0.028	10.8	4.0	– 4.4
37b	–12.8	–1.2	0.030	2.0	4.0	– 4.4
38a	–10.0	–6.4	0.026	6.0	5.4	– 3.6
38b	– 6.0	2.2	0.027	6.0	2.8	– 3.6
13	–46.4	–	–	–	12.0	0.0
34a	–35.6	–	–	–	4.0	– 9.0
34b	–22.8	–	–	–	9.4	– 5.0
2	–13.8	16.0	0.032	30.0	1.6	–10.0
7a	–24.0	20.0	0.044	30.0	6.0	– 8.8
7b	–26.0	12.4	0.042	15.6	8.4	– 8.6
31	– 9.0	20.0	0.031	34.1	2.0	–11.0
32	–14.2	23.0	0.036	31.6	4.0	–13.4
33	–19.6	18.0	0.038	26.0	7.2	–14.0
36a	–14.0	14.0	0.036	34.0	–4.0	–20.0
36b	–17.2	3.8	0.034	20.0	–2.0	–18.0
1	–23.0	–	–	–	21.2	– 1.8
29a	– 4.0	14.0	0.033	29.4	–4.0	–10.6
29b	– 3.4	9.6	0.029	24.0	–3.2	– 6.0
30a	– 3.8	0.0	0.026	32.8	–2.0	–10.6
30b	– 7.6	9.6	0.031	36.0	–2.0	–15.6
28a	– 6.4	0.0	0.031	12.0	–3.0	– 8.0
28b	– 6.0	4.0	0.033	18.0	4.0	–14.6
8a	–15.4	– 6.0	0.023	30.6	4.8	0.0
8b	–15.4	–15.4	0.022	24.0	4.0	0.0
35a	–12.0	– 2.0	0.015	29.0	4.0	– 9.4
35b	–14.4	–14.4	0.020	22.0	1.6	– 4.0
14	– 2.8	– 2.8	0.019	27.0	6.8	– 1.6
39a	– 4.0	– 2.0	0.019	40.8	2.6	– 5.0
39b	–10.0	–10.0	0.019	24.0	1.6	–12.8
3a	– 3.6	– 2.0	0.019	33.0	–2.2	– 8.3
3b	–	10.0	0.017	46.0	0.0	– 2.0

*Voltages are expressed in millivolts, and time in seconds.

the intrinsic upstroke is represented by a notch or node on the ascending limb of the chief deflection. In other complexes the downward movement amounts to several millimeters.

The curve from point *14* and most of the complexes of the curve from point *39* are similar to these just mentioned, but the initial upward movement is smaller, and its junction with the intrinsic deflection occurs, therefore, at a lower level. Most of the complexes of the curve from point *3* are of the normal type, but there are rhythmic variations, and a few resemble those just described.

Since space is not available for the reproduction of all the epicardial curves taken, they have been carefully measured. The measurements are incorporated in Table I, which gives the height of the initial summit, the level with reference to the base line at which the intrinsic upstroke begins, the amplitude of this upstroke, the range of the RS-T segment and T deflection in millivolts, and the time of the intrinsic upstroke with reference to the earliest ventricular deflection in standard Lead I in seconds. The range of the final deflections is given by two figures; the first gives the potential level of the first turning point, the second, the potential of the second turning point when such a point exists. Since the galvanometer connections were so made that relative negativity of the exploring electrode produced an upward movement of the string shadow, minus signs have been affixed to measurements which locate points above the base line, and ordinates which lie below this line are considered positive.

Experiment II (Dog 11).—In this instance the electrocardiographic study was made seventy-eight days after ligation of the anterior descending branch of the left coronary artery. The standard electrocardiogram taken at this time does not strongly suggest the presence of an infarct. Conspicuous Q deflections and inverted T-waves are present in all three leads. Three precordial leads were also taken. The copper disks which served as the exploring electrodes were sewn beneath the skin along a line which made an angle of about 30 degrees with the long axis of the body. The first of these disks was placed in the midline, the second 6 cm., and the third 12 cm. to the left of this line. The indifferent electrode was placed on the left hind leg. In the first and second precordial curves QRS begins with a downward excursion; in the third the initial movement is upward but small. These curves cannot be considered as characteristic of myocardial infarction. When the heart was exposed, an extensive, discolored, and somewhat depressed area was found on its anterior surface. In the center of this region the pericardium was adherent. Later examination showed that in the immediate neighborhood of the adhesions the infarct penetrated the ventricular wall over an area about one centimeter in diameter. The histological examination (carried out by Dr. C. V. Weller) of a block of tissue removed from this region showed an old fibroid scar which except for a few muscle fibers (probably Purkinje tissue) on the endo-

cardial side extended completely through the ventricular wall. The section also showed phagocytes containing old blood pigment, mucoid change in the scar tissue, early metaplasia of this tissue to cartilage,

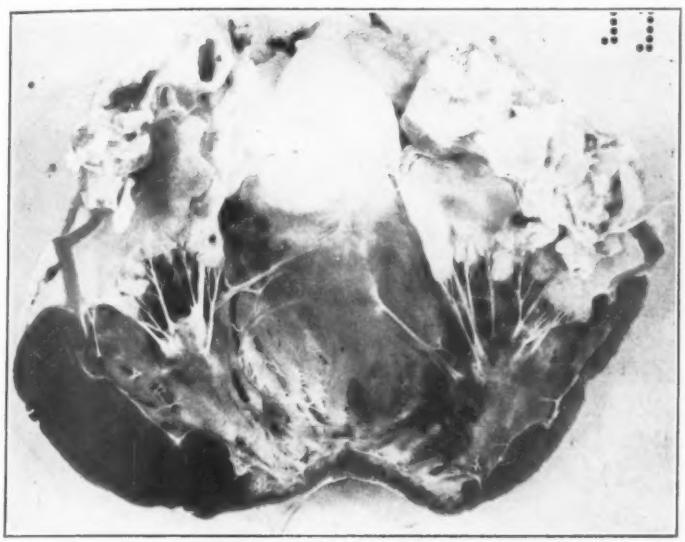

Fig. 4.—Experiment II (Dog 11). Photograph of the endocardial surface of the left ventricle.

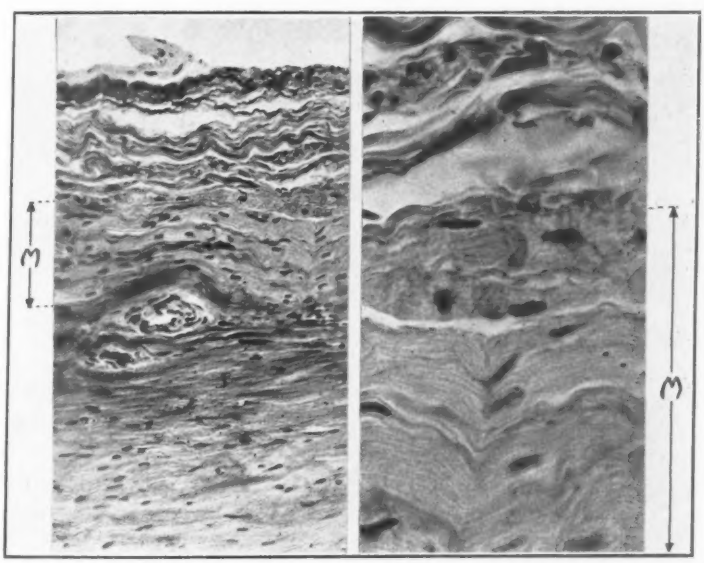

Fig. 5.—Experiment II (Dog 11). Photomicrograph of a section of the ventricular wall in the infarcted region. A thin layer of muscle fibers (*M*) lying just beneath the endocardium has escaped destruction. Low power on the left, and higher power on the right.

and small areas of lime deposit. A photograph of the endocardial surface of the left ventricle is reproduced in Fig. 4. It shows an extensive area of subendocardial fibrosis, which on the cut surface is seen to

involve the inner third or more of the ventricular wall. A photomicrograph of the section referred to is reproduced in Fig. 5.

Direct leads were taken from the points indicated on an outline drawing of the anterior surface of the heart shown in Fig. 6. Samples of the curves obtained are reproduced in Fig. 7.

The curves from points *9, 10, 11, 12, 13, 14, 15,* and *18* are of the normal type. The QRS group begins with a conspicuous downward movement which is immediately followed by an intrinsic upstroke of large amplitude, and the final portion of the ventricular complex has a normal contour. The curve from point *10* is very similar in general outline to that obtained at point *11,* but the initial downward movement is much smaller and amounts to less than 1 mm. At points *21* and *22* a sharp exploring electrode abolished the intrinsic deflection and yielded a purely monophasic response. At point *28* it gave a curve

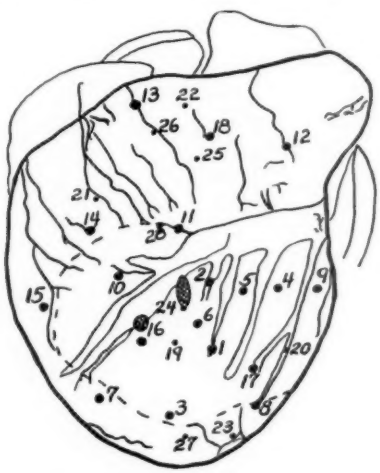

Fig. 6.—Experiment II (Dog 11). Outline drawing of the anterior surface of the heart showing the location of the points from which direct leads were taken. The crosshatched areas mark the location of pericardial adhesions. The broken line marks the limits of the discolored and depressed area mentioned in the text.

which, when compared with that obtained with the ordinary sponge-tipped electrode at nearby point *11,* shows a considerable decrease in the height of the intrinsic upstroke and a pronounced downward displacement of the RS-T segment. At point *10,* the changes in the ventricular complex induced by the sharp electrode were in the same direction but very small.

The curve from point *2,* where the infarct penetrated completely through the ventricular wall, is diphasic and consists of a tall unnotched initial summit followed by an inverted T deflection. There is no trace of an intrinsic upstroke, and no change whatever in the form of the ventricular complex occurred when the sharp electrode was employed. Curves of the same kind were obtained when this electrode was thrust into the left ventricular cavity at point *24* and at point *27.*

So far as the form of the QRS deflections is concerned, the curves from points *1*, *3*, *4*, *5*, *6*, *7*, and *8* resemble those obtained from the

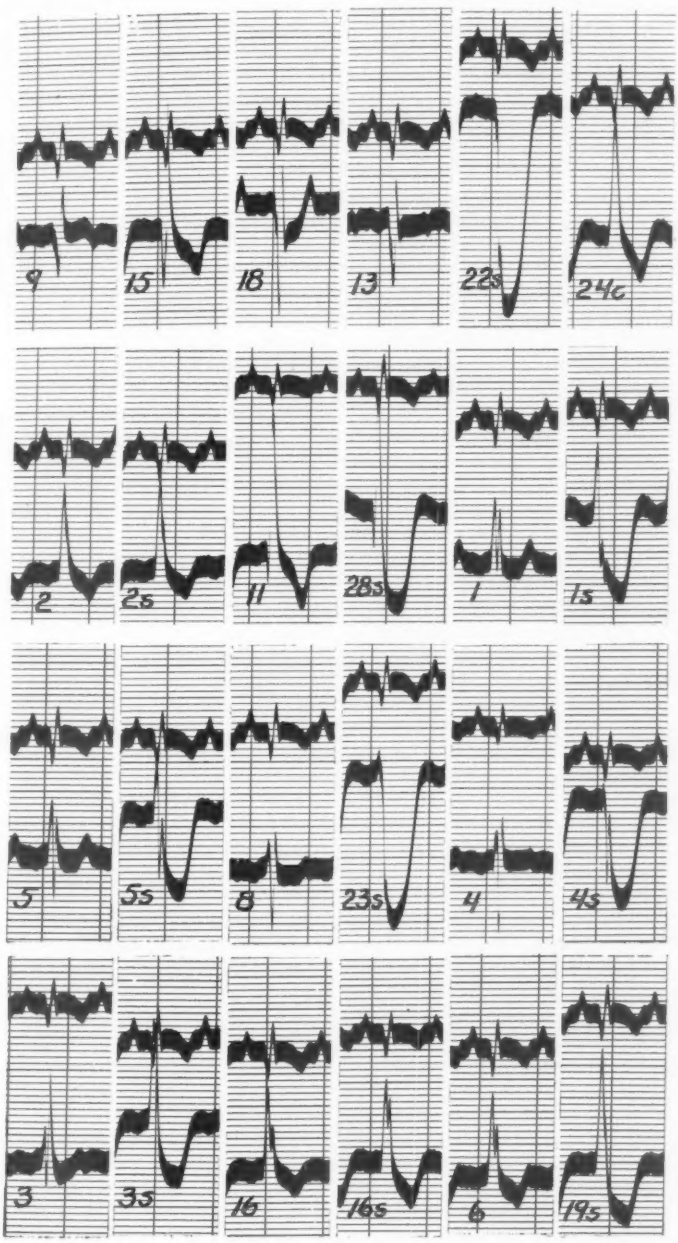

Fig. 7.—Experiment II (Dog 11). Direct leads from the points bearing corresponding numbers in Fig. 6. The upper curve in all records is standard Lead I. The conventions and additional data are the same as in the case of Fig. 3.

marginal portions of the infarcted region in Experiment I. They display both an initial summit and an intrinsic deflection and differ only

in respect to the size of these deflections and to the magnitude of the downward movement that separates them. The RS-T segment and T deflection, however, show no unusual features. At the majority of these points the injury inflicted by using a sharp electrode had no appreciable effect upon the preintrinsic portions of the ventricular complex. The intrinsic upstroke was reduced in height or abolished, and the post-intrinsic deflections were converted into a deep U-shaped depression. At points *3* and *7* and at point *19*, which is near point *6*, the curves obtained with the sharp electrode are exceptions to this rule. Except for the greater depression of the final portions of the ventricular complex, they resemble those obtained from the cavity of the left ventricle. It is possible that at these points the sharp electrode penetrated the living muscle and reached the layer of scar tissue beneath. The orig-

TABLE II

MEASUREMENTS OF THE CURVES OF EXPERIMENT II (DOG 11)*

POINT	VOLTAGE OF INITIAL SUMMIT	LEVEL OF INTRINSIC ONSET	TIME OF INTRINSIC ONSET	AMPLITUDE INTRINSIC DEFLECTION	RANGE OF FINAL DEFLECTION	
9	–	12.6	0.022	27.4	–1.8	0.0
10	–	2.6	0.003	47.2	15.0	0.0
10s	–	1.2	0.003	42.5	19.6	0.0
11	–	8.0	0.003	49.0	15.0	0.0
28s	–	6.0	0.003	40.0	30.0	–2.6
12	–	6.4	0.017	26.0	5.0	–0.8
13	–	20.0	0.020	28.6	4.6	0.0
14	–	13.8	0.005	50.0	14.0	0.0
15	–	15.6	0.007	52.8	12.0	0.0
18	–	34.0	0.021	41.6	13.6	–5.0
21s	–	–	–	–	55.0	0.0
22s	–	–	–	–	61.4	0.0
2	–25.0	–	–	–	6.0	0.0
2s	–26.0	–	–	–	7.0	0.0
24c	–33.0	–	–	–	11.2	–1.6
27c	–33.0	–	–	–	14.4	–0.6
1a	–17.2	1.0	0.022	14.0	2.0	–4.0
1b	–17.2	–1.6	0.020	14.0	2.0	–5.4
1s	–19.6	–	–	–	25.0	0.0
3a	– 5.6	12.4	0.018	34.0	3.6	–0.6
3b	– 7.0	6.0	0.020	32.0	5.0	0.0
3s	–24.0	–	–	–	18.0	0.0
4	– 6.0	20.0	0.022	29.6	1.0	0.0
4s	– 3.0	22.0	0.022	17.6	30.0	0.0
5	–14.0	11.0	0.025	18.4	2.0	–3.0
5s	–11.4	22.4	0.028	13.0	24.4	0.0
6	–23.0	9.4	0.023	7.0	6.0	–1.0
19s	–32.2	–	–	–	16.6	0.0
7	– 8.1	4.0	0.017	26.0	2.0	0.0
7s	–20.0	–	–	–	22.0	0.0
8	– 5.2	18.0	0.024	23.6	2.0	0.0
23s	– 4.0	–	–	–	47.2	0.0
16	–21.2	– 8.0	0.024	2.0	6.0	0.0
16s	–23.6	–11.2	0.021	4.4	11.6	0.0
17	– 3.6	14.0	0.023	21.6	5.2	0.0

*Voltages are expressed in millivolts, and time in seconds. When large rhythmic variations in the form of the ventricular complex occurred, the two complexes which differed most widely were measured. The two sets of measurements are designated by the letters *a* and *b*.

inal curve from point *16* shows a slight notch on the descending limb of the initial summit, but no other indication of the presence of an intrinsic deflection. The curve obtained with the sharp electrode shows only minor differences; the notch occurs at a slightly higher level, and T is somewhat more negative. It is, therefore, not certain that there was any living muscle at this point.

Measurements of the curves of this experiment are given in Table II.

COMMENT

The observations described show clearly that, when the whole thickness of the left ventricular wall is made up of scar tissue or dead muscle, the potential variations which occur at the epicardial surface of the region affected and those that take place in the neighboring portions of the ventricular cavity are practically identical. The potential variations occurring in the left ventricular cavity vary from point to point, but the general course of events is everywhere the same, and the curves obtained by leading from the epicardial surface of infarcts that extend completely through the left ventricular wall have, therefore, a characteristic outline. The initial and sole deflection of the QRS group is a tall summit, and T is usually inverted. There is no trace of a sudden intrinsic upstroke such as occurs in epicardial leads from healthy muscle.

It is apparent that, when the ventricular complexes recorded by leading from the epicardial surface and those obtained by leading from the nearest portion of the ventricular cavity are strikingly different, we may conclude that the intervening section of the ventricular wall is made up in whole or in part of muscle that is alive and is responding to the excitatory process. The electric forces generated by this muscle must be responsible for all the major differences observed. By comparing the ordinates of the one lead with the corresponding ordinates of the other, the general character of the time course of these electrical forces may be determined.

At the great majority of points on the anterior surface of the normal left ventricle, the potential with respect to an indifferent point becomes positive at the very beginning of the QRS interval, and this initial positivity increases more or less uniformly throughout the preintrinsic period. Since the ventricular cavity undergoes potential variations of the opposite kind at the onset of systole, it is evident that by far the greater part of the subendocardial muscle on the anterior wall of the left ventricle is already passing into the excited state when the QRS interval begins and that throughout the first part of this interval the electrical forces produced by the inner layers of muscle rapidly increase in magnitude. During this period the positivity of the epicardial sur-

face can continue to increase only as long as the growth of these forces is more rapid than the growth of negativity in the ventricular cavity. Later, when the inner negativity has reached its maximum and has begun to decline, the potential of the epicardial surface must rise unless the electromotive force across the ventricular wall is rapidly decreasing. When the excitation wave arrives at the epicardial surface in a given region, the electrical forces generated by its spread through that section of the ventricular wall are abruptly extinguished. The sudden decrease in the positivity of the epicardial surface thus brought about is represented in direct leads by the intrinsic deflection. The post-intrinsic QRS deflections of epicardial leads are similar to those inscribed during the same period in leads from the ventricular cavity.

It has been pointed out that the QRS group of many of the curves described displays both a prominent initial summit and a conspicuous intrinsic upstroke. The presence of the latter and the striking injury effects which appeared when a sharp electrode was pressed against the epicardial surface indicate that, in the regions from which these curves were obtained, the outer layers of muscle were alive and were responding to the excitatory process. During the inscription of the prominent initial summit the potential of the epicardial surface was negative and not, as a rule, materially different from that of the ventricular cavity. The presence of this deflection shows, therefore, that the innermost layers of muscle either produced electrical forces of subnormal magnitude or were activated abnormally late. In all probability both factors were operative, and we shall not attempt to reach a final decision as to which was the more important. The small initial summit which is not infrequently seen in direct leads from certain parts of the anterior surface of the normal heart is almost always followed by a large downward movement and a relatively late intrinsic deflection, and may logically be ascribed to late endocardial activation. In the case of the much larger initial summits under consideration, however, the situation is somewhat different. Very late activation of the endocardial surface should lead to equally late activation of the epicardial surface and should delay greatly the onset of the intrinsic upstroke. In some of the curves in question this deflection may be slightly delayed, but it does not appear to be greatly delayed in any. In many of these curves the downward movement which follows the initial summit is large and crosses the base line, whereas in others it is small or absent. It should be noted that in the former the intrinsic upstroke occurs relatively late while in the latter it is usually early. In the first case it usually begins after; in the second, before the negativity of the ventricular cavity has reached its maximum. It is obvious that a given rate of increase in the electromotive force across the ventricular wall will be much more likely to produce a downward movement when the negativity of the ventricular cavity is declining than when it is increasing.

In several experiments we attempted to determine whether section of the anterior subdivision of the left branch of the His bundle is followed by the appearance of an initial summit in direct leads from those portions of the ventricular surface to which it distributes the excitation wave. On the whole, these experiments were not very successful. In one or two instances a small initial summit appeared in a lead in which the QRS group originally began with a downward movement, or an initial summit originally present became slightly larger. None of the curves obtained displayed an initial summit large enough to be recognized at once as abnormal.

It is evident that in Experiment II curves of the kind in question were obtained only from those regions where the subendocardial muscle had been replaced by scar tissue and the subepicardial muscle was still living. Similar observations were made in other instances in which only the inner layers of muscle were infarcted. In such cases there is no reason to doubt that the magnitude of the electric forces produced by the subendocardial muscle were subnormal in magnitude. In Experiment I the muscle changes had not progressed far enough to enable us to determine easily the exact distribution of the infarcted tissue. The curves from points near the margin of the infarct are, however, strikingly similar to those obtained from regions where only the inner layers of muscle were involved in other experiments, and it does not seem probable that they had a different origin.

The observations made in Experiment II, and other experiments of a similar kind, present a very perplexing problem. Since the excitatory process spreads from the endocardial surface outward, it is difficult to see how it can reach the outer layers of muscle when the inner layers are dead or have been replaced by scar tissue. It is conceivable that it might reach this muscle by way of the normal parts of the ventricular wall beyond the boundaries of the subendocardial lesion, but this would require a great deal of time and must greatly delay the onset of the intrinsic deflection in the region affected. Since the intrinsic deflection is not greatly delayed, it would seem that the excitatory process must pass through the dead muscle or scar tissue, as the case may be. In this connection it is interesting that in Experiment II histological examination of the infarcted region showed that a thin layer of muscle fibers immediately beneath the endocardium was still intact. Dr. B. S. Oppenheimer was good enough to examine the sections which show these fibers and expressed the opinion that they were part of the Purkinje plexus. It is well known that Purkinje tissue tolerates oxygen want better than ordinary muscle, and this circumstance, together with the position of the left Purkinje plexus in relation to the blood of the left ventricular cavity, may explain its preservation in cases of the kind under consideration. Granting that much of the Purkinje network escapes in subendocardial infarcts, we are still unable to understand how

the excitatory process can cross the infarcted tissue unless we suppose that this tissue is penetrated by living Purkinje fibers or by surviving strands of ordinary muscle.

The flat or depressed RS-T segment and exaggerated T deflection encountered in direct leads from the margins of subacute infarcts of the left ventricle are obviously analogous to the so-called "coronary T-wave" seen in human coronary occlusion. In man these changes in the final portion of the ventricular complex may appear early, but they often reach the height of their development ten days or more after infarction occurs. In our animal experiments, on the other hand, they were never seen to persist in direct leads as long as twenty-four hours after coronary ligation. The reason for this difference between clinical and experimental myocardial infarction is not apparent.

While the flat or depressed RS-T segment may be a remnant of the injury effects that occur in the earliest stages of infarction, the T-wave changes are clearly due to disturbances that affect the return of the muscle from the active to the resting state. Since they are transient they cannot, like the QRS changes, be attributed to the disappearance of electrical forces normally produced by muscle that has been killed but must depend upon the generation of abnormal electrical forces in muscle that has been damaged. In leads from the ventricular cavity the final portion of the ventricular complex is usually represented by a U-shaped depression, which may be followed by a slight elevation above the base line. The occurrence of abnormally tall upright T deflections in epicardial leads indicates, therefore, that the magnitude of the electrical forces generated late in systole by the corresponding parts of the ventricular wall is abnormally great. The polarity of these forces is such as to make the epicardial surface negative, and it is possible that in the region affected the duration of the excited state increases from within outward. Smith[6] observed somewhat similar changes in the T deflection of direct leads accompanied by an increase in the duration of electrical systole and the length of the absolute refractory period when the muscle beneath the exploring electrode was cooled to a low temperature.

The close association in epicardial leads of final deflections of the kind in question and QRS deflections of the type discussed in preceding paragraphs suggests that the former, as well as the latter, may be in some way dependent upon effects produced in regions where only the inner layers of muscle are infarcted.

Throughout this discussion we have attempted to analyze curves inscribed in direct leads from an infarcted region by comparing them with those obtained from neighboring parts of the ventricular cavity. We do not wish to give the impression that infarction of the ventricular wall does not influence the potential variations occurring in the ventricular cavity. Theoretical considerations indicate that it must modify

them, and particularly those taking place at the nearest points. It is difficult, however, to demonstrate experimentally that this is the case, for it is evidently the magnitude rather than the general character of these variations that is altered. Changes in magnitude are not easily recognized without adequate controls, and to obtain such controls it is necessary to return the exploring electrode to precisely the same spot in the ventricular cavity that it previously occupied, or to allow it to remain in place throughout the period of observation. Because of the technical difficulties this question has not been investigated.

SUMMARY

Direct leads from the surface of infarcts that extend completely through the left ventricular wall yield ventricular complexes practically identical with those obtained by leading from the neighboring parts of the ventricular cavity. When the galvanometer connections are so made that relative negativity of the exploring electrode produces an upward deflection, these curves consist of a tall initial summit followed by a U-shaped final deflection which sometimes ends with a slight elevation above the base line.

In direct leads from regions where the inner layers of muscle are dead or have been replaced by scar tissue and where the outer layers are still living and responding to the excitatory process, the QRS group is characterized by the presence of both an abnormally large initial summit and a conspicuous intrinsic upstroke. A pronounced downward movement usually separates these two deflections but may be absent.

In the subacute stages of infarction the RS-T segment is often flat or depressed and the T-wave upright and abnormally large in leads from the marginal portions of the infarct. These changes in the final portion of the ventricular complex are usually associated with QRS deflections of the kind observed when only the inner layers of muscle are involved. Unlike these QRS changes, they persist for a very short time. They are due to disturbances affecting the recovery process in muscle that has been damaged, and not to the disappearance of electrical forces normally produced by muscle that has been killed.

We owe our thanks to Dr. John Nyboer, who made the measurements given in Tables I and II and to Dr. John Bugher, who was good enough to take for us the photomicrographs shown in Fig. 5.

REFERENCES

1. Wilson, F. N., Hill, I. G. W., and Johnston, F. D.: Am. Heart J. 9: 596, 1934.
2. Wilson, F. N., Hill, I. G. W., and Johnston, F. D.: (In press.)
3. Johnston, F. D., Hill, I. G. W., and Wilson, F. N.: (In press.)
4. Wilson, F. N., Johnston, F. D., Hill, I. G. W., and Grout, G. C.: Tr. A. Am. Physicians 48: 154, 1933.
5. Wilson, F. N., Johnston, F. D., and Hill, I. G. W.: Am. Heart J. 10: 176, 1934.
6. Smith, F. M.: Heart 10: 391, 1923.

THE RELATION OF THE POSITION OF THE HEART TO THE INITIAL VENTRICULAR DEFLECTIONS IN EXPERIMENTAL BUNDLE-BRANCH BLOCK*

PAUL C. FOSTER, PH.D.
NEW ORLEANS, LA.

ON THE basis of changes in the contour of experimentally produced canine bundle-branch block curves when the heart's position is altered, Ackerman and Katz[1] have recommended that no attempt be made to designate the bundle branch involved and that instead all such cases be called intraventricular block of the bundle-branch type. More recently Katz and his coworkers[2] have described two cases of left bundle-branch block (new terminology) in human beings in which changing the heart's position by altering the patient's posture resulted in electrocardiograms of an "indeterminate type."

We have repeated the experiments of Ackerman and Katz on thirteen dogs and two monkeys producing right block ten times and left block five times, displacing the hearts according to the technic of these authors and confirming the lesions by dissection. In confirmation of the above authors, we observed changes in the contour of the electrocardiograms including reversal in direction of QRS in Leads I or III, these changes being most easily produced by rotation of the heart on its long axis, simple displacement of the apex laterally or anteriorly being less effective. Typical results, using left branch block in the dog and monkey, are given in Fig. 1 and Fig. 2. Examples of reversal in Lead I and in Lead III are seen in each case.

The fact that right bundle-branch block in the dog gives curves, the initial deflections of which are typically inverted in all leads, and left branch block gives upward initial deflections in all leads, is now almost universally accepted. In exceptional cases the direction of the initial deflections may be oppositely directed in Leads I and III, or to use Lewis's terminology, the curves are "discordant." In Fig. 4 we have indicated by arrows the direction of the electrical axis in each of our experiments, and it will be seen that with right bundle-branch block "discordancy" occurred twice, once in Lead I and once in Lead III. All left bundle-branch curves were "concordant." Each of the monkeys, one with right and one with left block, gave "concordant" curves, thus being in agreement with the usual findings in the dog.

Although displacement of the heart by values equal to those used by Ackerman and Katz[1] altered the direction of the initial deflection at

*From the Laboratory of Physiology in the School of Medicine, Tulane University of Louisiana, New Orleans.

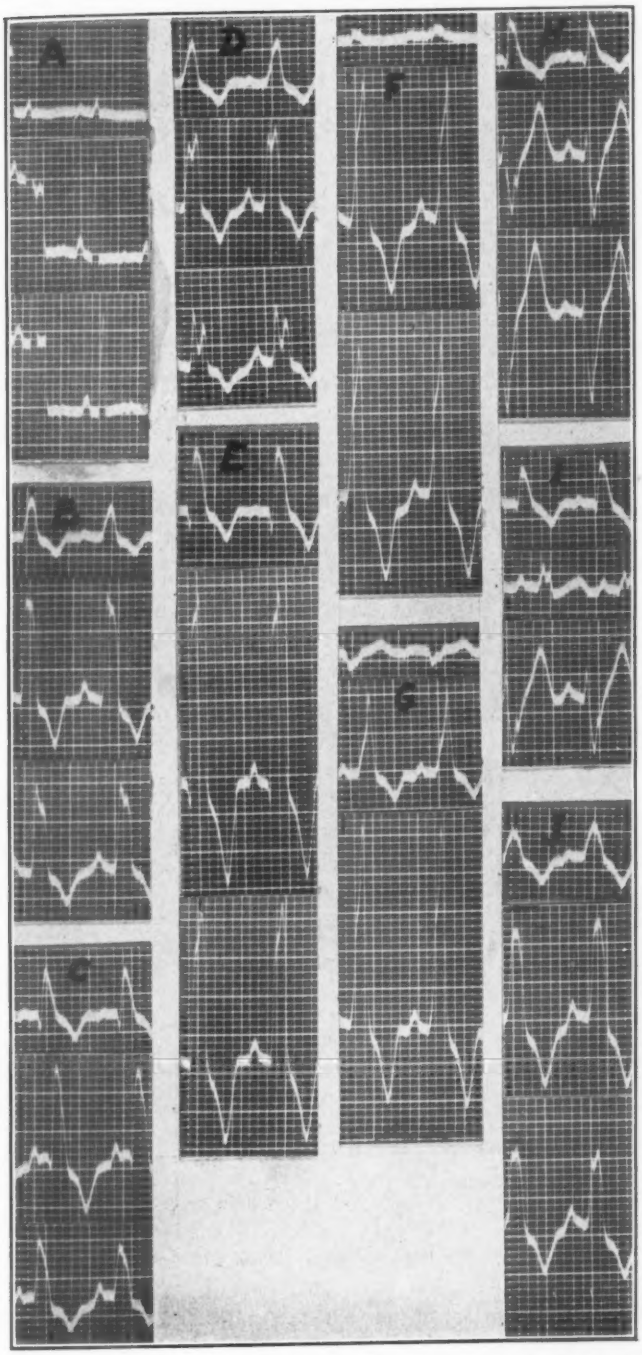

Fig. 1.—Effect of changing the position of the heart on the electrocardiogram in left bundle-branch block in the dog. (Curves in each block from top to bottom are Leads I, II, and III.)

A. Normal mechanism; chest open. B. After section of left bundle branch. Heart in normal position. C. Apex elevated 45°. D. Apex displaced left 30°. E. Apex displaced right 30°. F. Rotated left on long axis 30°. G. Rotated left 90° (as far as was possible). H. Rotated right 60° (as far as was possible). I. Rotated right 30°. J. Apex displaced left 30° and rotated left 30°.

times in Leads I or III in both right and left branch block, these curves simply became "discordant" curves of the same type and could hardly be confused with block of the opposite type. Fig. 4 shows the relation between the direction of the electrical axis and the direction of the initial deflections in each lead with the approximate range of human and canine branch block curves indicated. It is seen that the electrical

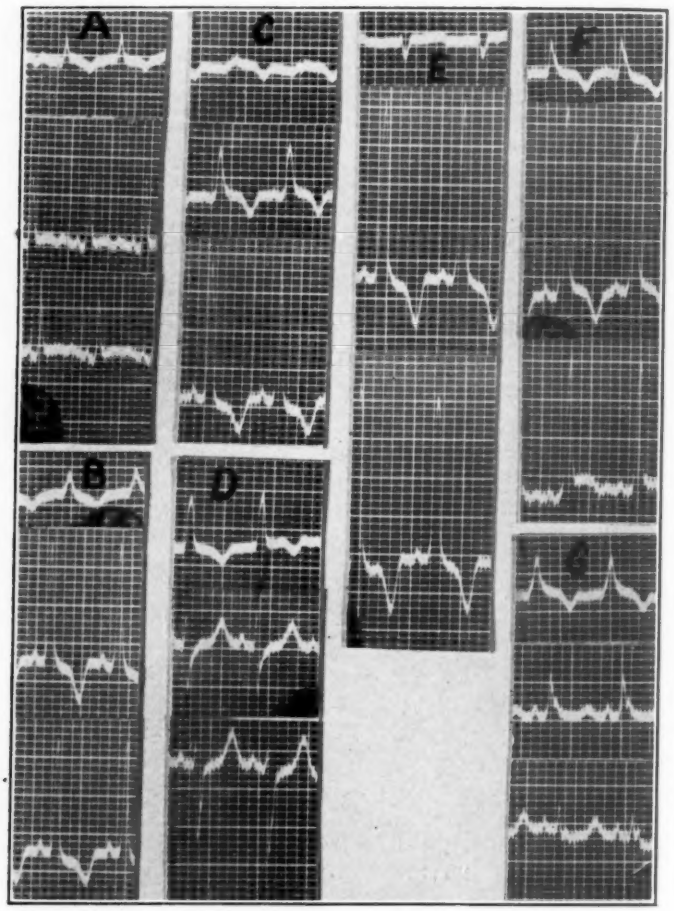

Fig. 2.—Effect of changing the position of the heart on the electrocardiogram of left bundle-branch block in the monkey. (Curves in each block from top to bottom are Leads I, II, and III.)

A. Normal mechanism; chest open.
B. After section of the left bundle-branch. Heart in normal position.
C. Apex elevated 45°.
D. Heart rotated right on long axis 45°.
E. Rotated left 45°.
F. Apex displaced right 30°.
G. Apex displaced left 30°.

axis must be displaced upwards of 180 degrees to change one type of curve into exactly that of the opposite type. That this is experimentally possible is illustrated in Fig. 3. In this case right bundle-branch block

with definitely downwardly directed complexes in all leads was made to resemble left bundle-branch block by displacing the apex until it pointed cephalad and rotating the heart so as to bring the right ventricle ventrad and the left dorsad as far as possible. Cardiac displacement of so ex-

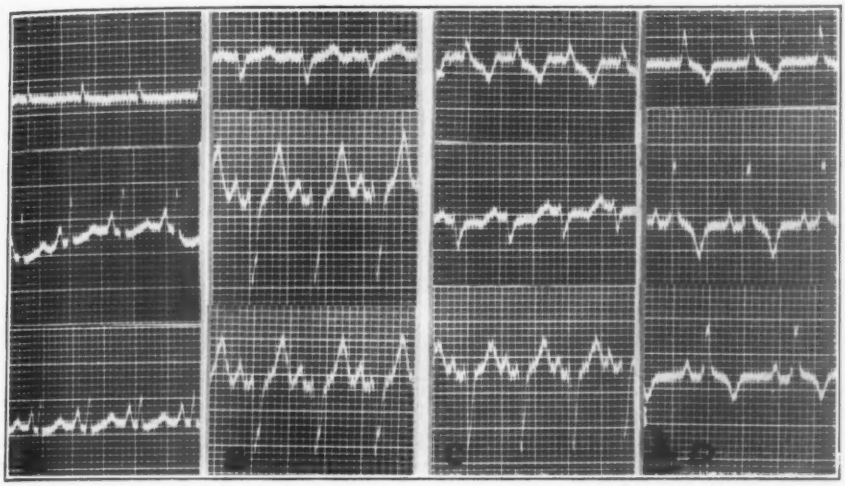

Fig. 3.—(Curves in each block from top to bottom are Leads I, II, and III.)
A. Normal mechanism. Chest open.
B. After section of the right bundle-branch.
C. Effect of displacing apex 15° upward, 30° to the left and rotating heart on the long axis 30° to the right.
D. Effect of completely inverting the position of the ventricles. Apex displaced anteriorly as far as possible, right ventricle rotated to left and left ventricle rotated to right as far as possible.

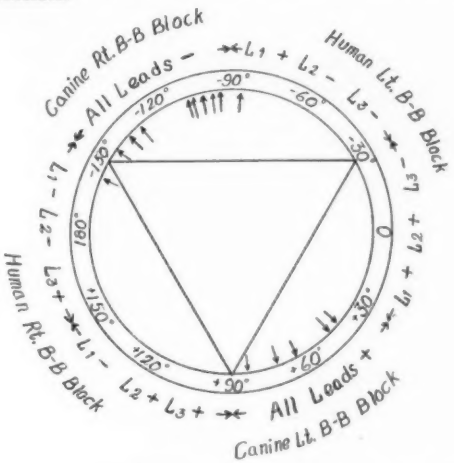

Fig. 4.—Relation between the direction of the electrical axis and the direction of the initial ventricular deflections in each of the standard leads. The small arrows indicate the direction of the axes in our cases of experimental branch block. The approximate range of axes in human and canine branch block is indicated.

treme a degree would be very unlikely to occur pathologically, and, if it did occur, it would hardly escape notice. We doubt if such experiments invalidate the use of the terms *right* and *left* bundle-branch block.

In the human cases cited by Kissin, Ackerman and Katz,[2] in which placing the patient on the left side resulted in the changing of curves from the type now generally considered to be typical of left bundle-branch block to an "indeterminate type," the electrical axis has been rotated to the right sufficiently that a downwardly directed wave in Lead III is now upwardly directed, but the axis still points left. We have seen the electrical axis in normal people rotate almost as much with changes of body position, but only in exceptional cases. That the position of the heart alters the contour of the waves in the electrocardiogram is no new idea, having been studied in Einthoven's laboratory[3] as early as 1913 and more extensively by Meek and Wilson[4] at a later date. Herrmann and Wilson[5] recognized that there must be fairly marked hypertrophy of a ventricle before a definite relation between the form of the ventricular complex and the relative weight of the two ventricles exists. Every electrocardiographer recognizes that with moderate axis deviation the body build of the patient as well as the body position while taking the record must be considered in evaluating such axis deviation. Thus, while admitting that alteration in the position of the heart may slightly modify the contour of the initial ventricular complexes, this, in most instances, we believe, would not lead to confusion in the bundle involved. In the two cases of Kissin, Ackerman, and Katz[2] the electrical axis at all times points so unmistakably to the left that on examining any of the curves the diagnosis of *left* bundle-branch block would appear to be the correct one.

SUMMARY

We see no valid experimental evidence that warrants the abandonment of the use of the terms *right* and *left* in describing intraventricular block of the bundle-branch type.

REFERENCES

1. Ackerman, W., and Katz, L. N.: Reversal in Direction of the QRS Complex of Experimental Right Bundle-Branch Block with Changes in the Heart's Position, AM. HEART J. 8: 490, 1933.
2. Kissin, M., Ackerman, W., and Katz, L. N.: The Effect of the Heart's Position on the Electrocardiographic Appearance of Bundle-Branch Block in Man, Am. J. Med. Sc. 186: 721, 1934.
3. Einthoven, W., Fahr, G., and deWaart, A.: Über die Richtung und die manifeste Grösse der Potentialschwankungen im menschlichen Herzen und über den Einfluss der Herzlage auf die Form des Electrokardiogramms, Arch. f. d. ges. Physiol. 150: 275, 1913.
4. Meek, W. J., and Wilson, A.: The Effect of Changes in Position of the Heart on the QRS Complex of the Electrocardiogram. Arch. Int. Med. 36: 614, 1925.
5. Herrmann, G. R., and Wilson, F. N.: Ventricular Hypertrophy: A Comparison of Electrocardiographic and Postmortem Observations, Heart 9: 91, 1921-1922.

THE ANATOMICAL AND HYDROSTATIC BASIS OF ORTHOPNEA AND OF RIGHT HYDROTHORAX IN CARDIAC FAILURE*

WM. DOCK, M.D.
SAN FRANCISCO, CALIF.

THE accumulation of blood and edema fluid in the dependent parts of the lung is recognized as a common consequence of passive hyperemia due to heart failure and as a predisposing cause of terminal pneumonia and of hydrothorax. However, the hydrostatic analysis of pulmonary venous drainage has not been used in accounting for orthopnea and the preponderance of right-sided pleural transudates, although these phenomena have excited curiosity and experimental study leading to varied and often rather complicated explanations. Widely current theories ascribe right hydrothorax to the pressure of the right auricle on the right pulmonary vein, and orthopnea to postural facilitation of thoracic and diaphragmatic movement or to changes in vital capacity when blood shifts into the lungs from the dependent parts of the body. In this paper I shall discuss the gravitational relations of the pulmonary outflow to the left ventricle, and indicate that most of the blood reaching the left ventricle from the lungs must run uphill whenever the patient lies on his back or his right side, but that ventricular filling from the pulmonary bed is aided by gravity when the shoulders are elevated or when the patient is in the left lateral position. The relation of these facts to orthopnea and to the frequency of right hydrothorax is obvious, since venous pressure must be higher in order to force blood upward and high venous pressure causes more rapid transudation, leading both to pulmonary edema with impaired respiration and to pleural effusion.

METHODS

Data on the relation of the blood in the lungs to the left ventricle were obtained from a study of recorded drawings of cross-sections of the adult thorax and from roentgen ray films. The object of the measurements was to determine the geometric center of the left ventricular cavity and of the lungs, and the vertical distance between these two points in erect and supine positions.

The lung fields of two sets of cross-sections[1, 2] were copied on sheets of uniform thickness, and the skin surface behind was marked on each sheet. The center of the left ventricle was placed by inspection; its distance anterior to the skin surface measured; and this distance laid off on each sheet. Lines parallel to the line of support behind were drawn through the level of the center of the left ventricle and

*From the Department of Medicine, Stanford University School of Medicine, San Francisco.

at 2 cm. intervals anterior and posterior to it in order to divide the lung fields into zones centering 1, 3, 5, 7, 9, etc., cm. anterior to or posterior to the center of the ventricle. The lung fields were cut out and weighed, and the weights of the pairs at each level together with the distances of the sections caudad to the apex were used to calculate the center of gravity. The weights multiplied by their distances from the apex were summed by Simpson's rule and divided by the weights summed in the same way. This gives the approximate distance of the center of gravity below the apex, and subtracting this from the distance from the apex to the center of the left ventricle gives the relation of heart to center of mass of the lungs. The sections were then cut up into transverse zones, each group of zones weighed; and the weights, together with the average distances posterior to the ventral lung margin, were used to calculate the distance from the anterior lung margin to the center of gravity. Thus the position of the center of gravity of the lungs and its relation to the center of the left ventricle were determined in two planes.

Six-foot roentgenograms of the chest, 2 sec. exposures at the end of a normal inspiration, were made in the anteroposterior line erect and left lateral erect and supine. Posterior displacement of the heart in the latter seemed negligible; the diaphragms were higher. The lateral erect and the anterior projections were copied and used for further work. On the right lung field of the anterior projection, vertical lines were laid off at half-inch intervals, and the ends of these lines projected into the lateral view of the lung fields. A series of sections were drawn to correspond to anteroposterior sections through the right lung. These were fastened together with mounting tissue so as to form a compressed reconstruction of the right lung. This was suspended by a needle through one corner and a plumb-line, dropped from the needle, was used to locate the line of its center of gravity. This was repeated from two other points of suspension, and the center of gravity located where the lines intersected. This was transferred to the lateral projection as indicating the location of the center of the lung. The position of the left ventricular center was fixed by inspection. The vertical line was drawn parallel to the edge of the film, which had been in a vertically aligned holder.

The results are given in Table I. It is apparent that in asthenic persons (such as Braune's[1] cadaver) the distance between heart and lung centers is greatest in the caudad-cephalad line, but in hypersthenics, such as this hypertensive patient, the anteroposterior distance is very great as compared with the caudad-cephalad difference. For adult men of 160-180 cm. height it appears that 10 degrees change in the position of the axis of the trunk in the vertical plane will cause 1 cm. change in the pulmonic venous pressure needed to maintain constant cardiac output.

TABLE I

THE RELATIVE POSITIONS OF THE CENTERS OF MASS OF THE LUNG AND OF THE LEFT VENTRICLE

SOURCE OF DATA	DISTANCE FROM CENTER OF LUNG TO LEFT VENTRICLE			
	CHEST WIDTH (CM.)	CEPHALAD-CAUDAD (CM.)	ANTERO-POSTERIOR (CM.)	TOTAL ON CHANGE FROM RECUMBENT TO ERECT (CM.)
Normal, cadaver (Braune[1])	23	5.7	3.4	9.1
Normal, cadaver (Eycleshymer[2])	25	3.8	5.0	8.8
Normal, roentgen films	29	4.7	4.3	9.0
Hypertensive, roentgen films	30	2.9	6.8	9.7

DISCUSSION

On inspection of the thoracic viscera of embalmed cadavers, of cross-sections, or of anteroposterior roentgen ray projections (Fig. 1) of the chest, it is evident that the center of the right lung lies nearly 10 cm. below the left ventricle in the right lateral recumbent position, and that of the left lung is only 2 to 5 cm. below the left ventricle in the left lateral position. Since cardiac patients, often conscious of the apex beat, tend to roll toward their right sides in order to rest their backs, it is only natural that throughout the day the pulmonary venous pressure on the right should average several centimeters of water more than the left. In left heart failure and in mitral stenosis,

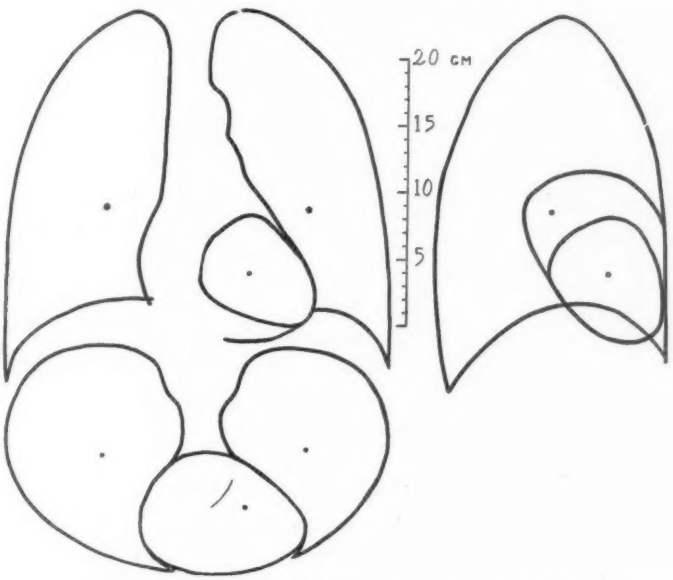

Fig. 1.—The frontal and lateral silhouettes of a normal subject, from roentgen ray films, and the thoracic cross-section drawn from measurements of the films and actual cross-sections.[3] The centers of the lungs and of the left ventricle are indicated by dots; the outlines of the left ventricles and of the mitral aperture are indicated also.

pressure in the left auricle is more altered than in the right, and it is not credible that the slightly engorged right auricle can compress pulmonary veins which have a much higher internal pressure. It seems logical therefore to ascribe the frequent occurrence of right hydrothorax to the fact that pressure in the veins of the right lung must be higher than in the left, since both drain into a common chamber and the right is on the whole more often dependent, and when dependent is much lower than the left. Then, too, the left lung, especially when the heart is enlarged, has less lower lobe surface than the right, and it is the lower lobes which have the highest venous pressure.

That orthopnea cannot be due to high venous pressure in the systemic circuit is apparent in dealing with cases of severe tricuspid valve disease or cases of obstruction to the superior cava. Other evidence against that theory has been presented by Hamilton,[3] by Weiss,[4] and by Calhoun.[5] In patients with ascites or with large pleural exudates orthopnea is occasionally present, and in these cases it must be ascribed not to changes in the lungs primarily, but to the fact that purely thoracic breathing is more effective in the erect position because the fall of the diaphragm lengthens the thoracic compartment available for expansion. When the diaphragm is pressed up by high intraabdominal pressure in the recumbent position or when in the erect position it sags under the weight of several liters of pleural fluid, it is probable that the patient will find it easier to breathe if he sits up. In cardiac patients with hydrothorax, engorged livers, and tympanitic bowels these factors also are operative and may contribute to the preference for the orthopneic posture.

Primarily the patient with heart failure suffers from the high venous pressure behind an inefficient ventricular chamber or a damaged auriculoventricular valve. As the efficiency of the heart's mechanical function fails, venous pressure rises until it reaches a level sufficient to evoke an approximation of the normal minute volume of cardiac output. In the right ventricle of dogs and of men an increase of 1 cm. of water pressure in the veins forces an increase of about 10 per cent in cardiac output, and the study of pulmonary blood flow rate[6] and of vital capacity[7] in hyperthyroidism indicates that the left ventricle responds similarly to slight changes in venous pressure. When the heart fails, a rise of 5, 10, or even 20 cm. of water in venous pressure with a normal or subnormal minute output of blood from the heart indicates how greatly ventricular efficiency has failed—in a normal heart such a rise in venous pressure would cause 50, 80, or 150 per cent rise in minute volume. The degree of impairment in efficiency may be very different in the right and in the left side of the heart, and there often is little change in venous pressure in systemic veins in patients with mitral stenosis or with hypertension, aortic insufficiency, or some other factor which precipitates left ventricular failure and rise in pressure in pulmonary veins. The latter is measured indirectly by the slowing of flow through the dilated lung veins and manifests itself by lowering vital capacity and causing lung engorgement demonstrable in roentgenograms or on auscultation. The general level of pulmonary venous pressure depends then on the level of cardiac output to be maintained, on the level of ventricular efficiency, and on the gravitational gradient between the venous ends of the lung capillaries and the left ventricle. Change of posture is not without influence on the level of cardiac

output, since this may rise 5 to 30 per cent on the assumption of a recumbent position,[8] but there is simultaneously an increase in efficiency of left ventricular systole, due to the fall in diastolic pressure. When the cardiac output in experimental animals[9] is increased without any decrease in peripheral resistance, there is an increase of 10 to 15 per cent in the blood held in the heart chambers and lung vessels due to a 50 per cent increase in cardiac inflow, but one hesitates to accept Hamilton's view that the decrease in vital capacity occurring when normal subjects assume a supine posture is due to the increased cardiac inflow. This only averages a small percentage and is offset by a fall in peripheral resistance and hence a more efficient left ventricular emptying.

When an adult lies down, the blood in his lung capillaries must, as these studies of lung mass and ventricular position indicate, run upward from 3.5 to 7 cm. in order to reach the left ventricle; when he is erect the blood runs downward from 3 to 5.7 cm. before it reaches the ventricle. Since cardiac output depends on the maintenance of an adequate pressure at the venous inlet of the ventricles, and since it is not diminished but may be slightly increased on lying down, the pressure in the ventricle during diastole must be at least as great when the person is recumbent as when he is erect.

To maintain a given level of left ventricular output, the pressure in pulmonary veins will necessarily be from 7.5 to 10 cm. greater in the recumbent than in the erect position. This, of course, refers to the average, but, since in fact most of the lung is distant from the actual center of mass, what actually is meant is that the proportion of the lung in which the venous pressure must be higher than that in the left ventricle is far larger in the recumbent than in the erect posture. Hence, when the venous pressure, elevated as a result of heart failure, is further augmented as a result of lying down, the vital capacity is diminished, pulmonary edema more readily occurs and the Hering-Breuer reflexes become more urgent. Respiration becomes shallower and less effective, and dyspnea, which was absent in the sitting posture, becomes progressively more embarrassing. Even in normal individuals there is evidence that the blood content of the lungs is increased on lying down and that all the change in vital capacity is due to this hyperemia.[3] But this is not a shift in blood "stored" in the lower extremities to blood "storage" in the lungs. The blood is merely trapped in the distended veins in dependent parts of the lungs, and, if the general level of the lung veins in relation to the point of outflow into the ventricle were not altered, the lungs would not be affected by change in posture. In theory, cardiac patients should then be less dyspneic when prone than when recumbent, but when prone respiration is effected only by raising the

heaviest parts of the trunk. However, Weiss noted that orthopneic patients when inclined forward had higher vital capacity and less dyspnea than when the angle of the body to the horizontal was the same with the back dependent.[4] This observation can be explained only by the anatomic and hydrostatic relations of heart and lungs.

In all discussions of cardiac dyspnea it must be borne in mind that the subjective sensation is not due merely to overventilation. The cardiac patient is often so uncomfortable that he seeks the relief given by sitting up, when the actual minute volume of ventilation is only one-half or one-third as great as that which causes consciousness of respiratory effort in a normal individual during mild exercise at high altitudes. The respiratory effect of lung hyperemia cannot be explained by the increased minute volume of respiration necessitated by heightened Hering-Breuer reflexes and the resulting rapid, shallow, inefficient respiration. Nor is it due to reduced vital capacity, for the tidal air of a dyspneic cardiac patient may be only one-sixth of his vital capacity, while that of an athlete, exercising without respiratory distress, often is one-fourth or one-third the vital capacity. Since the athlete's respiratory rate is also greater than the dyspneic cardiac patient's, it is obvious that the awareness of respiratory effort which makes a recumbent patient sit up is due neither to increase in volume, in rate, nor in percentage of vital capacity used in respiration. The loss of lung elasticity due to hyperemia and the consequent rise in intrathoracic pressure[10, 11] causes the cardiac patient to increase the muscular element in expiration to a much greater degree than occurs in the athlete who is sustaining a tolerable, constant load of physical effort, even though his respiratory rate, minute ventilation, and ratio of $\frac{\text{tidal air}}{\text{vital capacity}}$ are all higher than those of the cardiac patient (Table II). The necessity of using muscular effort in expiration, because of bronchospasm, emphysema with loss of lung elasticity; or experimental narrowing of the chief airway always results in consciousness of respiratory activity, and this is what is meant by dyspnea. The subjective phenomenon which is known as dyspnea, and which often leads to orthopnea in cardiac patients, is due then chiefly (as Wiggers[12] has emphasized) to the need for expiratory effort imposed by loss of lung elasticity. The rise in pulmonary venous pressure of recumbent cardiac patients undoubtedly adds to the stiffness of the lung and diminishes the recoil effect which normally causes expiration. In this way, as much as or more than by reducing vital capacity, it makes the patient aware of the effort of breathing. Observation of overbreathing by patients breathing against the slight but unfamiliar resistance of a spirometer, in tests of basal metabolism, arouses a suspicion that in the cardiac patients who occasionally show low arterial acidity, consciousness of respira-

TABLE II

	MEN WITHOUT DYSPNEA		CARDIAC PATIENTS WITH DYSPNEA IN P.M.		EXERCISING NORMAL AT 70% OF WORK TOLERANCE
	A.M.	P.M.	A.M.	P.M.	
Respiratory rate in minutes	15	16	20	23	23
Total minutes ventilation	6.65 l	7.00 l	8.00 l	9.26 l	42.00
Percentage of normal A.M. minutes ventilation	100%	105%	120%	139%	630%
O_2 intake per minute	250 c.c.	275 c.c.	250 c.c.	275 c.c.	1750 c.c.
R.Q. (from experience with normal and cardiac diets)	0.82	0.86	0.82	0.90	0.95
CO_2 output per minute	205 c.c.	237 c.c.	205 c.c.	247 c.c.	1660 c.c.
Percentage of normal A.M. CO_2 output	100%	115%	100%	120%	810%
Arterial CO_2 tension, mm. Hg	40.5	36.1	45.3	43.3	38.0
Alveolar CO_2 content, per cent	5.3	4.8	6.0	5.7	5.00
Essential ventilation of alveoli per minute	3.66 l	4.71	3.23	4.07	33.2
Ventilation efficiency $\frac{\text{Essential ventilation}}{\text{Total ventilation}}$	55%	67%	41%	44%	79%
Percentage of daily rise in essential ventilation		29%		26%	
Arterial pH	7.435	7.480	7.37	7.39	7.35
Per cent of normal P.M. H ion concentration	111%	100%	129%	123%	135%
Tidal air	443 c.c.	438 c.c.	400 c.c.	403 c.c.	1830 c.c.
Vital capacity	3960 c.c.	3900 c.c.	2400 c.c.	2220 c.c.	4200 c.c.
Diurnal decrease vital capacity		60 c.c.		180 c.c.	
Ratio $\frac{\text{Vital capacity}}{\text{Tidal air}}$	8.9	8.9	6.0	5.5	2.3

NOTE.—From data of Cullen, Harrison, and coworkers (Arch. Int. Med. 53: 724, 1934, and J. B. C. 83: 545, 1929) and for exercise, from L. J. Henderson's data on A.V.B. (who had the same resting arterial blood findings as Cullen's normals) in *Blood*, Yale Press, 1928. At sea level ventilation adequate to wash out CO_2 raises alveolar O_2 tension so high that blood is practically saturated with O_2, and therefore CO_2 output and alveolar tension determine the ventilation requirement. The table shows that normal persons, in spite of a daytime rise in CO_2 output, ventilate their lungs more effectively and lower arterial CO_2 tension and acidity, while cardiac patients with a tendency to dyspnea in spite of bed rest have more acid blood and higher CO_2 tension, effect less reduction in acidity and CO_2 tension by day than normal persons, and have a rise in total ventilation out of proportion to their increased CO_2 output in the evening. All of this points to (1) less efficient pulmonary and nervous mechanism for ventilating the lungs of the cardiac, and (2) less sensitive respiratory center in the cardiac. Comparison with the normal man, exercising vigorously but well below his tolerance for continued effort, shows that the dyspneic cardiac patient breathes no faster, moves only one-fourth as much air each minute, and uses only half as much of the available vital capacity in breathing as does a normal man under conditions in which respiratory distress may not be appreciable. Awareness of respiratory distress in the cardiac patient is apparently not due simply to an elevated rate, or elevated minute volume of respiration, or to decrease in ratio of vital capacity to tidal air.

tory effort causes overventilation and not, as has been suggested, that overventilation is a significant element in causing dyspnea and orthopnea. An examination of the data published by Cullen and his coworkers, as well as those of others who have examined the blood gases of dyspneic cardiac patients, indicates that overventilation is not the rule (using arterial CO_2 tension and pH as indices) but occurs only occasionally (Table II). Diminished sensitivity of the respiratory center is usually found in patients suffering from dyspnea at rest or orthopnea.

Orthopnea, then, is due to the patient's being more aware of and disturbed by his breathing when he lies down than when he sits up. He is aware of his breathing because respiration is labored, that is, because expiration is no longer passive but involves muscular effort, and not simply because he breathes as often or has as high a ratio of tidal volume to vital capacity as normal persons have during the unconscious hyperventilation due to exercise. The breathing is labored because the lungs are relatively inelastic and the normal intrathoracic negative pressure and elastic recoil are decreased. The rise in pulmonic venous pressure necessitated by recumbent posture can contribute to lung inelasticity and raise respiratory effort above the threshold of consciousness.

SUMMARY

When an adult of average size is recumbent, the blood flowing from the pulmonary venous bed must be lifted from 4 to 7 cm. against the force of gravity in order to fill the left ventricle; but when the body is erect, the pulmonary outflow descends from 3 to 5.5 cm. to reach the left ventricle. Thus the pulmonary venous pressure which is adequate in the erect position to maintain a given level of left ventricular filling and cardiac output is lower than that needed to maintain the same level of cardiac output, when the individual is recumbent, by the pressure represented by a column of blood 7.5 to 10 cm. high. In the same way, the pulmonary venous outflow from the right lung of an adult in the right lateral recumbent posture must be lifted 10 cm. or more to reach the left ventricle, that from the left lung, when in the left lateral position, need be lifted only 5 cm. Therefore, the average venous pressure needed to maintain the flow of blood will be much higher in the right lung than in the left, even if the individual spends equal periods lying on the two sides. In patients, like many cardiac patients, who favor the right lateral decubitus, this difference in average pressure between the venous beds in the lungs will be increased. It is suggested that these hydrostatic factors of anatomical origin are of paramount importance in causing orthopnea and the preponderance of right pleural transudation in patients with heart failure.

REFERENCES

1. Braune, W.: Topographischer-anatomischer, Atlas, Tables X, XI, XII, XIII, XIV. Leipzig, 1888, Veit & Company.
2. Eycleshymer, A. C., and Schoemaker, D. M.: A Cross-Section Anatomy, Sections 21-28, New York, 1911, D. Appleton-Century Company.
3. Hamilton, W. F.: Dyspnea and Some Mechanisms of Respiratory Regulation, M. Ann. District of Columbia **1:** 321, 1932.
   Hamilton, W. F., and Morgan, A. B.: Mechanism of the Postural Reduction in Vital Capacity in Relation to Orthopnea and Storage of Blood in the Lungs, Am. J. Physiol. **99:** 526, 1932.
4. Weiss, S., and Robb, J. P.: Cardiac Asthma (Paroxysmal Cardiac Dyspnea), J. A. M. A. **100:** 184, 1933.
5. Calhoun, J. A., and others: Orthopnea: Its Relation to Ventilation, Vital Capacity, Oxygen Saturation and Acid-base Condition of Arterial and Venous Blood, J. Clin. Investigation **10:** 833, 1931.
6. Blumgart, H. L., Gargill, S. L., and Gilligan, D. R.: The Circulatory Response to Thyrotoxicosis, J. Clin. Investigation **9:** 69, 1930.
7. Lemon, W. S., and Moersch, H. J.: Basal Metabolism and Vital Capacity, Arch. Int. Med. **33:** 130, 1924.
8. Schneider, E. C., and Crampton, C. B.: The Effect of Posture on the Minute Volume of the Heart, Am. J. Physiol. **110:** 14, 1934.
9. Drinker, C. K., Churchill, E. D., and Terry, R. N.: Volume of Blood in Heart and Lungs, Am. J. Physiol. **77:** 596, 1926.
10. Christie, R. V., and Meakins, J. C.: Intrapleural Pressure in Congestive Heart Failure, J. Clin. Investigation **13:** 323, 1934.
11. Prinzmetal, M., and Kountz, W. B.: Intrapleural Pressure in Orthopnea, Proc. Soc. Exper. Biol. & Med. **31:** 610, 1934.
12. Wiggers, C. J.: Dyspnea: Physiology in Health and Disease, Philadelphia, 1934, Lea & Febiger, pp. 410, 411.

FOLLOW-UP STUDY OF SIXTY-FOUR PATIENTS WITH A RIGHT BUNDLE-BRANCH CONDUCTION DEFECT*†

FRANCIS CLARK WOOD, M.D., WILLIAM A. JEFFERS, M.D.,
AND CHARLES C. WOLFERTH, M.D.
PHILADELPHIA, PA.

IN JUNE, 1930, a woman, aged sixty-one years, came in for routine cardiovascular study, "just to be sure everything was all right." Her electrocardiogram showed a bizarre QRS complex (Fig. 1*A*). She had no other evidence of cardiovascular disease: no symptoms, normal blood pressure (105 systolic and 65 diastolic), normal orthodiagram, no murmurs, and no signs of congestive heart failure. She has been studied at intervals since then, the last time on May 10, 1935. Her present cardiovascular status is the same as it was five years ago. The electrocardiogram is unchanged (Fig. 1*B*). She had been known to us for many years prior to 1930 and had never had any cardiac symptoms. We suspect, therefore, that she may have had this deformity of her QRS complex for years before it was found.

When this patient first appeared, we were engaged in studying the electrocardiograms of a group of 1,000 college students and 145 business executives. One student and two business men, with no other evidence of cardiovascular disease, showed this same type of electrocardiogram. Consequently, in 1930, we collected all similar tracings from our files and have periodically followed the cardiovascular status of the patients with them, by means of clinical methods, electrocardiograms, and orthodiagrams. We have added to the group all patients with this type of tracing who have presented themselves since that time‡ and now have a total of sixty-four. The present paper is based upon an analysis of these cases with special reference to their cardiovascular status when first seen and their subsequent clinical course.

I. *Characteristics of the Electrocardiogram.*—The terminal downward deflection of QRS in Lead I and usually its final upward deflection in Lead III are widened, slurred, and notched. The duration of QRS is 0.12 second or more. In the uncomplicated case, the tracing is otherwise normal. Certain variations are seen, which have been classified into four types by Bayley.[1] Wilson[2] and his coworkers have

*From the Edward B. Robinette Foundation, Medical Clinic, Hospital of the University of Pennsylvania.

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‡Dr. William B. Porter, of Richmond, and Dr. James W. Esler, of Washington, have each supplied us with one.

presented evidence that these phenomena in the QRS complex are due to right bundle-branch block. Our observations[3] based upon the time relation of the dynamic events in the two ventricles support this view: right ventricular contraction was delayed in the four patients which were studied. However, histological studies of these cases are not available, and we do not know whether the block of the right bundle branch is complete.

II. *Analysis of the Cardiovascular Findings at the First Examination, of Sixty-Four Cases With a Right Bundle-Branch Conduction Defect.*—Table I tabulates the results. Group A contains twenty patients who when first seen, showed no evidence of heart disease or hypertension, except the QRS deformity. The evidence of peripheral

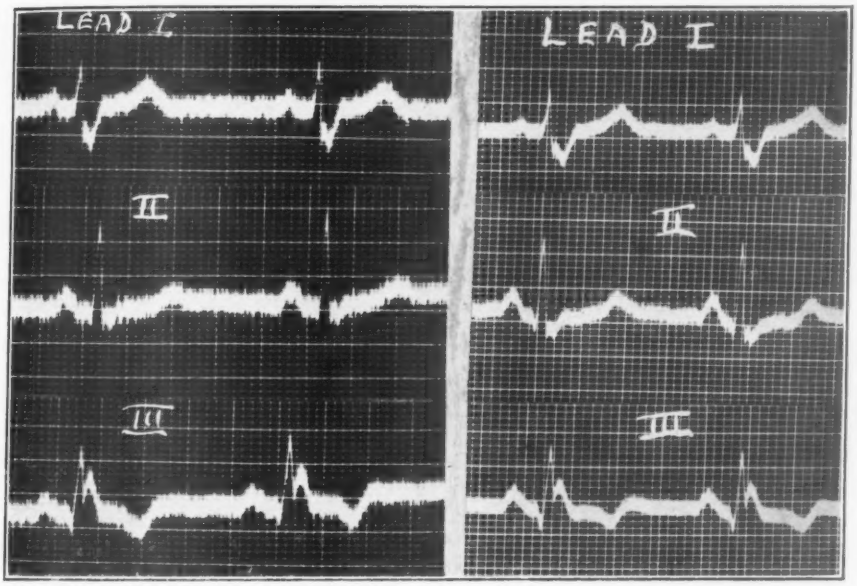

Fig. 1.—*A*, electrocardiogram of a woman, aged sixty-one years, taken on June 23, 1930. She showed no signs or symptoms of cardiovascular disease. The S-wave in Lead I and the R-wave in Lead III are widened and slurred. The QRS interval is 0.13 second. The electrocardiogram is otherwise normal.

B, electrocardiogram of the same patient taken on May 10, 1935, showing no definite change. Her present cardiovascular status is the same as it was five years ago. She has no cardiac symptoms, normal blood pressure, normal orthodiagram, no murmurs, and no signs of congestive heart failure.

vascular sclerosis in all but one of these patients was not out of proportion to age. Nineteen had no peripheral vascular symptoms; one, aged sixty-three years had intermittent claudication. Group B contains fifteen cases which have been classified as having "no very marked evidence of heart disease." Group C contains twenty-nine cases which showed definite evidence of heart disease in addition to the electrocardiographic findings. Fourteen of the sixty-four had other significant electrocardiographic abnormalities besides the QRS

deformity (T-wave inversion, 5 cases; P-R prolongation, 6 cases; auricular fibrillation, 2 cases; paroxysmal ventricular tachycardia, 1 case). If these fourteen cases are removed from the two groups, two from B and twelve from C, fifty remain, of which twenty had no other evidence of heart disease except the QRS deformity. This is a rather striking proportion, especially since all but two of these patients received complete cardiovascular study. Bayley[1] has reported that many patients with bundle-branch block show no physical signs of heart disease. However, these patients did not even have any significant cardiac symptoms.

TABLE I

CLASSIFICATION OF 64 CASES OF RIGHT BUNDLE-BRANCH CONDUCTION DEFECT ON THE BASIS OF THE FIRST EXAMINATION

A. No other evidence of heart disease or hypertension		20
B. No very marked evidence of heart disease		15
Nothing but slight cardiac enlargement	5	
Nothing but vague precordial pain	3	
Nothing but a systolic murmur	1	
Nothing but T-2 inversion	1	
Nothing but P-R prolongation	1	
Hypertension—no enlargement, angina or failure	4	
C. Definite signs of heart disease		29
Etiology not clear	5	
Congenital	2	
Rheumatic	3	
Syphilitic	1	
Hypertension with enlargement, angina or failure	11	
Coronary disease without hypertension	7	

III. *The Age Incidence.*—Table II gives these data. Three-fourths of the patients were over fifty years of age when they were first seen. This fact is of importance with regard to life expectancy. It also suggests that many of the individuals in Group A may have a degenerative lesion in the conduction system, rather than a congenital or an inflammatory one.

TABLE II

AGE OF 64 PATIENTS WITH RIGHT BUNDLE-BRANCH CONDUCTION DEFECT AT TIME OF FIRST EXAMINATION

	0-10 YR.	11-20 YR.	21-30 YR.	31-40 YR.	41-50 YR.	51-60 YR.	61-70 YR.	71-80 YR.
Group A No other evidence of heart disease or hypertension		2	1		2	6	7	2
Group B No very marked evidence of heart disease					1	5	6	3
Group C Definite signs of heart disease	1	1	2	2	4	6	8	5
Total	1	3	3	2	7	17	21	10

IV. *Follow-Up Studies.*—Table III tabulates the follow-up of the cases in the three groups.

TABLE III

FOLLOW-UP OF 64 CASES OF RIGHT BUNDLE-BRANCH CONDUCTION DEFECT

FOLLOW-UP	LOST	LESS THAN 1 YR.	1 YR.	2 YR.	3 YR.	4 YR.	5 YR.	6 YR.	7 YR.	11 YR.	TOTAL
Group A. No evidence of heart disease or hypertension at first examination, except the QRS deformity	1	2		3*	4	4	5	1			20
Group B. No very marked signs of heart disease except the QRS deformity	2	1	1	3†	2	2	2		1	1	15
Group C. Definite signs of heart disease, in addition to the electrocardiographic findings	7	7	3	3	3	3	2		1		29
	10	10	4	9	9	9	9	1	2	1	64

*One case, followed for two years, has not been seen for the last three years.
†One case, followed for two years, has not been seen for the past twelve months.
We have been in contact with all the rest of these patients until the present time, except the ten in the "Lost" column, and eight who have died (see text).

Group A: Four patients in this group have shown a definite change in their status during the follow-up period. One, a man seventy-two years old, developed coronary occlusion and died after having been followed for two years. A second patient, a man aged fifty-seven years, after having been followed for four years, suffered a coronary occlusion in April, 1935, but survived. The other two, males, aged fifty-seven and fifty-nine years, followed for two and five years, respectively, have developed hypertension without enlargement of the heart, congestive failure, or cardiac symptoms. The other patients who have been followed have not developed any new signs or symptoms; they still have no evidence of heart disease, except the QRS deformity.

Group B: Two individuals in this group have shown a definite change in their status during the follow-up period. One man whose only abnormality was a P-R interval of 0.26 second survived a prostatectomy, developed hypertension, and died of apoplexy, at the age of seventy-eight years, after having been followed for three years. The second patient, a sixty-four-year-old woman with hypertension, after being followed for seven years without change, developed hyperthyroidism, congestive failure, and auricular fibrillation. She has

recently had a subtotal thyroidectomy and is recovering. The other cases that have been followed have shown no definite change. One patient, a physician, has been seen at intervals for eleven years since the QRS deformity was first discovered. He has had slight cardiac enlargement and many extrasystoles at each examination. He is now seventy-two years old and is still engaged in active practice.

Thus, in these first two groups of cases, which showed nothing immediately serious in the original findings, except the QRS deformity; twenty-two of thirty-five patients have been followed from two to eleven years without definite change. Three have been lost. Four have developed serious trouble, but in only two of these was the cause of the trouble intrinsically cardiac.

Group C: Six of the twenty-nine patients are known to have died. Four succumbed during the first year of follow-up: one from sarcoma and three from heart disease. Two died during their third year of follow-up: one from carcinoma and one from heart disease. Ten have lived from two to seven years and are still living. These patients fared no worse than one might expect them to on the basis of their cardiovascular lesions, without reference to the QRS deformity.

Of the entire group of sixty-four cases, eight are known to be dead. Ten have been lost. More than half have been followed from two to eleven years and are still alive; more than one-third have been followed for four years or more and are still alive.

DISCUSSION

There are many published reports which deal with the cardiovascular status and prognosis of patients with intraventricular conduction defects.[4] The following are representative excerpts from them: Graybiel and Sprague,[4a] on the basis of a series of 395 cases, state that "bundle-branch block almost invariably indicates serious organic disease of the heart, usually coronary disease; the average duration of life of the 223 fatal cases in this series, after discovery of the conduction fault, was one year and two months, but eighty-five other patients are still alive after an average of two years and eleven months. . . . . With few exceptions, the patients still living are either seriously limited in their activity or are actually in some stage of cardiac decompensation. Among the fatal cases, the chief cause of death, where this is known, has been, in nearly every instance, cardiac failure. . . . . Partial bundle-branch block must be regarded clinically as equally significant with complete bundle-branch block, the prognosis in both being essentially the same." King,[4b] on the basis of 150 cases, states: "The prognosis . . . . . is of extreme gravity in bundle-branch block in general." Herrmann and Ashman[4c] write: "Prognostically electrocardiographic findings indicating defective in

traventricular conduction, especially if persistent, are significant of grave myocardial damage." Thus, a review of the literature leaves one with the impression that most cases with an intraventricular conduction defect have serious heart disease, and have, on the average, less than two years to live. It has been recognized that some patients live considerably longer,[5] but it is probably the general feeling that they are exceptional.

Two main facts emerge from our study of this particular group of sixty-four patients with a right bundle-branch conduction defect: (1) *A smaller proportion of them have serious heart disease than the literature on bundle-branch lesions would lead one to expect,* and (2) *the presence of this electrocardiographic abnormality per se, does not seem to add materially to the gravity of prognosis.*

We have found in the literature three references which deal with the clinical status of patients with this type of electrocardiogram. Bayley[1] reviewed seventy cases, together with 103 cases of left bundle-branch block. In speaking of both types together, he states, "The average patient with bundle-branch block shows little evidence of cardiovascular disease on routine physical examination, and one is frequently surprised when the electrocardiogram discloses a serious conduction defect." He does not discuss separately the clinical aspects of his cases of right bundle-branch block, nor compare them with left-sided block. Thus, he leaves unanswered a question which we have likewise failed to answer: How does the cardiovascular status of patients with this right bundle-branch defect compare with that of patients with conduction disturbances of other types? Bayley publishes no follow-up studies. He does not state that any of his cases have no evidence of heart disease except the electrocardiographic abnormality. Von Deesten and Dolganos[6] in a paper entitled "Atypical Bundle-Branch Block With a Favorable Prognosis" report five patients with the QRS deformity which is the subject of our paper. None of their cases presented evidence of serious heart disease, and four of them were followed for eleven, eight, four, and three years, respectively, without much change. Oppenheimer, in a recent personal communication, stated that a study by himself, Rothschild and Mann,[7] which appeared in abstract in 1925 also dealt with this type of case. Nine of their ten patients showed no downward progress during the period of follow-up. The reports of von Deesten and Dolganos and of Oppenheimer, Rothschild, and Mann are the only papers we have found which view an intraventricular conduction defect with optimism. Their observations leave one with the impression, however, that the cardiovascular status of these patients is better than a larger series of cases shows it to be.

Several other points seem worth emphasizing:

1. Of the fourteen patients with other significant electrocardiographic abnormalities, in addition to the QRS deformity (such as T-wave inversion, P-R prolongation, auricular fibrillation, and paroxysmal ventricular tachycardia) twelve had definite evidence of cardiovascular disease at the first examination in addition to the electrocardiographic phenomena. Only two patients did not, and one of them developed hypertension and died. It seems, therefore, that T-wave inversion, and the other abnormalities referred to, have their usual significance when they appear in these cases. Three of the sixty-four patients had a significant Q-wave[8] in Lead III; one case in Group B and two in Group C. Many other patients just escaped having a significant Q_3 by virtue of a small upward deflection preceding the downward deflection of QRS.

2. Chest leads were taken in twenty cases. Bizarre curves were obtained. In some instances, especially with the anterior electrode in the third left interspace near the sternum (Fig. 2*A*), the tracings bore a superficial resemblance to those obtained in acute coronary occlusion. It should be emphasized that bundle-branch block (a) may appear during an attack of acute coronary occlusion and mask the electrocardiographic signs of this lesion[9] or (b) may produce RS-T interval deviations in the absence of recent cardiac infarction which may be mistakenly interpreted as evidence of coronary occlusion.

3. We have seen this QRS deformity make its appearance in three patients while they were under our observation.[10] The first was a forty-nine-year-old man, who had no evidence of cardiovascular disease when first seen in 1930. In 1930, 1931, and 1932 his tracing was normal. In 1933, 1934, and 1935 it showed the QRS deformity. There were no symptoms of onset that we could elicit. The cardiac shadow has been slightly enlarged throughout. He is classified in Group B. The second case was that of a man, aged sixty-nine years, with anginal pain and definite coronary artery disease. In 1932 and 1933 the QRS complex was normal. In 1934 the QRS deformity appeared and persisted until his death from carcinoma of the head of the pancreas. There were no clear-cut symptoms accompanying the appearance of the QRS deformity. He is classified in Group C. The third patient was a man fifty years old who developed this QRS deformity during a fatal attack of acute coronary occlusion.[9a]

4. There were three cases in which the QRS deformity appeared and disappeared from time to time[4c, 11] (Fig. 2*B*).

5. These cases of right bundle-branch defect differ in several respects from the cases with short P-R interval, QRS deformity and good prognosis reported by Wolff, Parkinson and White,[12] which may be due to a functioning bundle of Kent:[13] (a) The P-R interval is

not short. (b) In the three patients mentioned above, in whom the QRS deformity appeared and disappeared, the P-R interval and the initial deflection of QRS did not change (Fig. 2*B*). (c) The widening and slurring involve the terminal portion of QRS, not its initial deflection. (d) In one patient who had a paroxysm of tachycardia, the QRS complex deformity was present before, during, and after the paroxysm. In the cases reported by Wolff and his associates, it tended to disappear during paroxysmal arrhythmia.

6. The physical signs of this lesion are not diagnostic. Many patients have split heart sounds. However, the frequency of this finding in the absence of QRS prolongation makes it an unreliable diagnostic sign.[3]

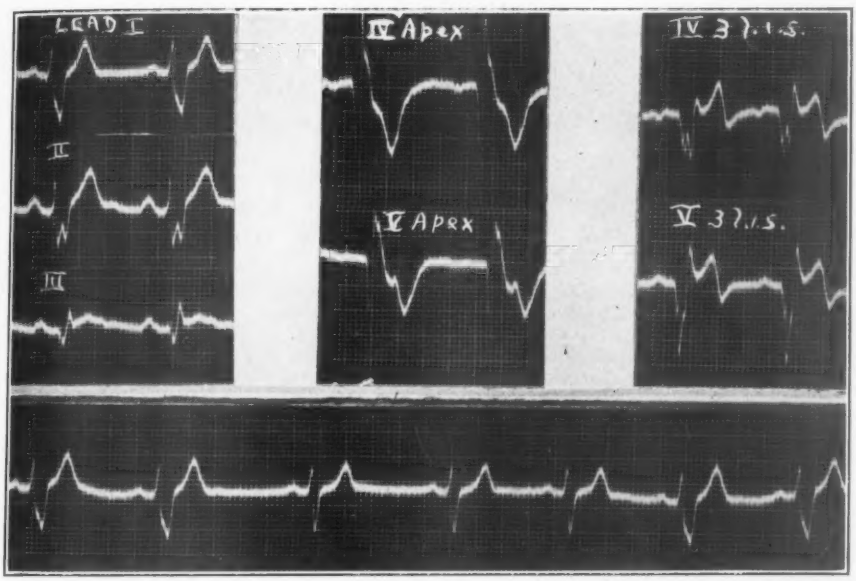

Fig. 2.—Electrocardiograms of a boy aged nineteen years, with a right bundle-branch defect, a rough systolic murmur and thrill at the fourth left interspace near the sternum, slight enlargement of the heart, blood pressure of 110/60, fairly good exercise tolerance, and no signs of active cardiac disease. He probably has a congenital interventricular septal defect.

A, shows the limb leads and the chest leads numbered as in previous publications.[14] At the extreme right are Leads IV and V, taken with the anterior chest electrode in the third left interspace, near the sternum. These tracings present an appearance which might be mistakenly interpreted as evidence of recent cardiac infarction.

B, shows Lead I in the same case. The QRS deformity disappeared for three beats. The P-R interval and the initial deflection of QRS did not change.

7. Bayley[1] has classified his cases of right bundle-branch block into four groups. Our cases can be similarly classified: Type I, 23 cases; Type II, 6 cases; Type III, 32 cases; Type IV, 3 cases. However, correlations between this grouping and other factors, such as age, sex, heart size, or degree of cardiac damage, are not striking.

8. There are forty-six males and eighteen females in the group.

9. The frequency of this electrocardiographic abnormality in the general population is not known. Bayley's observations suggest that the term "rare" type of bundle-branch block is a misnomer. Our cardiovascular survey of 1,300 unselected college students* and 145 unselected business executives over forty-five years of age has some bearing upon this point. None of the 1,300 college students had left bundle-branch block; two of the 1,300 showed this right bundle-branch defect. One is classified in Group A and one in Group C. Among the 145 business executives over forty-five years of age, none had left bundle-branch block; five showed this right bundle-branch defect. Two of these are classified in Group A, two in Group B, and one in Group C. Although three of these five had other evidences of heart disease when first seen (one case, T_2 inversion; the second, slight cardiac enlargement; the third, moderate cardiac enlargement), none of them had cardiac symptoms. All have been followed for five years without any striking change. On the basis of these observations it would seem likely that there are a considerable number of people over forty-five years of age with this QRS deformity, who are blissfully unaware of its existence. Most of them will lead a life of average comfort and happiness unless someone discovers it and makes them give up part of their pleasure and freedom. Since we have not restricted the activity of any patients in this group on strictly electrocardiographic grounds, their longevity cannot be ascribed to a life of rigorous self-denial.

SUMMARY

1. Sixty-four patients with electrocardiograms of the type shown have been studied carefully and many of them followed over a period of years.

3. If fourteen cases with other significant electrocardiographic abnormalities are excluded, fifty cases remain. Of these, twenty showed no evidence of heart disease when first seen, except the QRS deformity, thirteen showed relatively minor evidences of heart disease, and seventeen showed definite evidence of heart disease.

3. Follow-up: The patients with little or no other evidence of heart disease did well on the whole, when one considers that three-fourths of them were over fifty years old when first seen. Those with definite evidence of heart disease seemed to follow the clinical course expected of their lesions without reference to the abnormality of the QRS complex.

4. When this type of electrocardiogram is found in a patient with no other evidence of heart disease, it is not necessarily an ominous

*One thousand students were studied in 1929 and an additional 300 in 1934.

prognostic sign. Its presence per se in a group of patients does not seem to add materially to the gravity of their prognosis.

5. These facts seem worthy of emphasis since most patients with intraventricular conduction defects have been regarded as having serious heart disease and a grave prognosis.

REFERENCES

1. Bayley, R. H.: The Frequency and Significance of Right Bundle-Branch Block, Am. J. M. Sc. **188:** 236, 1934.
2. Wilson, F. N., Johnston, F. D., Hill, I. G. W., Macleod, A. G., and Barker, P. S.: The Significance of Electrocardiograms Characterized by an Abnormally Long QRS Interval and by Broad S-Deflections in Lead I, AM. HEART J. **9:** 459, 1934.
3. Wolferth, C. C., and Margolies, A.: Asynchronism in Contraction of the Ventricles in the So-Called Common Type of Bundle-Branch Block: Its Bearing on the Determination of the Side of the Significant Lesion and on the Mechanism of Split First and Second Heart Sounds, AM. HEART J. **10:** 425, 1935.

4 a. Graybiel, A., and Sprague, H. B.: Bundle-Branch Block: An Analysis of 395 Cases, Am. J. M. Sc. **185:** 395, 1933.

4 b. King, J. T.: Bundle-Branch Block: A Case Analysis With Especial Reference to Incidence and Prognosis, Am. J. M. Sc. **187:** 149, 1934.

4 c. Herrmann, G., and Ashman, R.: Partial Bundle-Branch Block: A Theoretical Consideration of Transient Normal Intraventricular Conduction in the Presence of Apparently Complete Bundle-Branch Block, AM. HEART J. **6:** 375, 1931.

4 d. Willius, F. A.: Clinical Features of Cases Exhibiting Electrocardiograms Conforming to Those of Experimental Complete Bundle-Branch Block, AM. HEART J. **1:** 576, 1926.

4 e. Cowan, J., and Bramwell, J. C.: The Clinical Aspect of Bundle-Branch Block, Quart. J. Med. **19:** 95, 1925.

4 f. Herrick, J. B., and Smith, F. M.: Observations on Block of the Branches of the Auriculoventricular Bundle, Am. J. M. Sc. **164:** 469, 1922.

4 g. Talley, J. E., and Reed, O. K.: A Study of Twenty-Eight Cases of Bundle-Branch Block, AM. HEART J. **1:** 262, 1926.

4 h. Oppenheimer, B. S., and Rothschild, M. A.: Electrocardiographic Changes Associated With Myocardial Involvement, J. A. M. A. **69:** 429, 1917.

4 i. Hill, I. G. W.: Bundle-Branch Block: A Clinical and Histological Study, Quart. J. Med. **23:** 15, 1930.

4 j. Granger, A. S.: The Clinical Significance of Bundle-Branch Lesions, California & West. Med. **24:** 626, 1926.

5 a. Levy, J. R.: Valeur Prognostique des Anomalies Permanentes de L'Electrocardiogramme Ventriculaire, J. méd. franç. **19:** 438, 1930.

5 b. Krumbhaar, E. B.: Editorial Note, Am. J. M. Sc. **188:** 235, 1934.

5 c. Bach, F.: On the Clinical Significance of Right Bundle-Branch Block, Quart. J. Med. **23:** 261, 1930.

5 d. Carter, E. P.: Clinical Observations on Defective Conduction in the Branches of the Auriculo-Ventricular Bundle, Arch. Int. Med. **13:** 803, 1914.

5 e. Bishop, L. F., and Bishop, L. F., Jr.: Bundle-Branch Block of Unusual Duration, J. A. M. A. **98:** 398, 1932.

6. Von Deesten, H. T., and Dolganos, M.: Atypical Bundle-Branch Block With a Favorable Prognosis, Am. J. M. Sc. **188:** 231, 1934.
7. Oppenheimer, B. S., Rothschild, M. A., and Mann, H.: Cardiographic Differentiation of a Sub-Group of Intraventricular Block With Observations on the Prognosis, J. Clin. Investigation **1:** 592, 1925.
8. Pardee, H. E. B.: The Significance of an Electrocardiogram With a Large Q in Lead III, Arch. Int. Med. **46:** 470, 1930.

9 a. Wolferth, C. C., and Wood, F. C.: Further Observations Upon the Use of Chest Leads in the Electrocardiographic Study of Coronary Occlusion (Case II), Med. Clin. North America **16:** 161, 1932.

9 b. Wolferth, C. C., and Wood, F. C.: Acute Cardiac Infarction Involving Anterior and Posterior Surfaces of the Left Ventricle: Electrocardiographic Characteristics (Case 1, Fig. 1-A), Arch. Int. Med. **56:** 77, 1935.

10. Morris, R. S., and McGuire, J.: Transient Complete Bundle-Branch Block, Am. J. M. Sc. **184**: 202, 1932.
11 a. Stenstrom, N.: Further Experience on Incomplete Bundle-Branch Block in Man, Acta med. Scandinav. **67**: 353, 1927.
11 b. Carr, F. B.: Functional Bundle-Branch Block, New England J. Med. **209**: 1101, 1933.
12. Wolff, L., Parkinson, J., and White, P. D.: Bundle-Branch Block With Short P-R Interval in Healthy Young People Prone to Paroxysmal Tachycardia, AM. HEART J. **5**: 685, 1930.
13 a. Holzmann, M., and Scherf, D.: Ueber Elektrokardiogramme mit verkurzter Vorhof-Kammer-Distanz und positiven P- Zacken, Ztschr. f. klin. Med. **121**: 404, 1932.
13 b. Wolferth, C. C., and Wood, F. C.: The Mechanism of Production of Short P-R Intervals and Prolonged QRS Complexes in Patients With Presumably Undamaged Hearts: Hypothesis of an Accessory Pathway of Auriculoventricular Conduction (Bundle of Kent), AM. HEART J. **8**: 297, 1933.
14. Wood, F. C., Bellet, S., McMillan, T. M., and Wolferth, C. C.: Electrocardiographic Study of Coronary Occlusion: Further Observations on the Use of Chest Leads, Arch. Int. Med. **52**: 752, 1933.

THE RELATIONSHIP OF HEART-BLOCK, AURICULOVENTRICULAR AND INTRAVENTRICULAR, TO CLINICAL MANIFESTATIONS OF CORONARY DISEASE, ANGINA PECTORIS, AND CORONARY THROMBOSIS

JORGE SALCEDO-SALGAR, M.D.,
BOGOTA, COLOMBIA, S. A.,
AND
PAUL D. WHITE, M.D.,
BOSTON, MASS.

INTRODUCTION

FOR many years investigators have studied the functional and structural pathological conditions that disturb the conduction system of the heart to cause heart-block. The use of electrocardiography has resulted in a great advance in the detection of heart-block of various kinds and grades. On the other hand, our understanding about certain anatomicopathological lesions of the conduction system has remained obscure; there is a discrepancy between the two sets of data in the present state of our knowledge, a gap which will eventually be lessened or abolished after a more extensive study of the correlation of the clinical manifestations of heart-block with structural lesions and functional defects in the conduction system.

While awaiting the time when we shall have a complete understanding of the relationship between heart-block (of various types and grades) and pathological changes in the conduction system of the heart or in the blood vessels supplying it, we should make use of any clues that we have already at hand in assessing the relationship between heart-block and coronary disease. Such clues we possess in the determinations of the incidence of the known clinical manifestations of coronary disease, namely, paroxysmal angina pectoris and coronary thrombosis, in cases with heart-block, and, conversely, of the incidence of heart-block of various types in cases with paroxysmal angina pectoris or coronary thrombosis. In the present study we have made such analyses; that is, of the relationships between the clinical manifestations of coronary disease and the various types of heart-block.

A delay in auriculoventricular conduction time exceeding 0.20 of a second for the P-R interval of the electrocardiogram is considered, in this study, as indicative of auriculoventricular block. We have

divided intraventricular block into three groups, in accordance with the electrocardiographic variations (and not necessarily in accordance with structural lesions of the conduction system). Lesser degrees of intraventricular block are considered present when there exists a widening of the QRS complexes which exceeds 0.11 second, with slurring and notching but without the characteristics of full bundle-branch block. Full left bundle-branch block is considered present in those cases in which, with the duration of the ventricular complexes more than 0.11 second, there is left axis deviation. Full right bundle-branch block shows wide QRS waves with right axis deviation. In accordance with the latest studies of Wilson and his coworkers on bundle-branch block we have included under right bundle-branch block cases whose electrocardiograms show very wide S-waves in Lead I and under left bundle-branch block cases whose electrocardiograms show wide upright QRS waves in all leads; the former are common, the latter rare, a fact that tends somewhat to equalize the numbers of right and of left bundle-branch block. It was once believed that there existed a very great preponderance of left bundle-branch block.

In the present analysis we have not included the rare cases of apparent bundle-branch block (wide QRS waves) with short P-R intervals, since these cases are to be classified, not as intraventricular block, but rather as very early spreading of the impulse to one ventricle or the other.[1, 2]

LITERATURE

Here and there in the literature there have been brief observations as to the presence of heart-block in coronary disease and as to the presence of clinical evidences of coronary disease in heart-block, but the correlation of the two relationships has not, so far as we have discovered, been the subject of special study such as we have made and are reporting here. The practical importance of the study is evident, as well as is its academic interest.

A few references to large series of cases of angina pectoris and coronary thrombosis and of heart-block that have been published are as follows:

Levine[3] in 1929 noted disorders of heart rhythm in cases of coronary thrombosis, especially those that concern premature beats and the sudden development of heart-block, which may be related to the localization of the infarct. He said that in general the appearance of heart-block during coronary thrombosis is an unfavorable sign, though he believed that a slight delay in conduction was not important. He reported that the immediate mortality in his series of 143 cases of coronary thrombosis was 53 per cent and that the average duration of life was twenty-four months in the patients who survived the im-

mediate illness; the average age was 54.7 years; he did not give data concerning the relative prognosis of coronary thrombosis with auriculoventricular and with intraventricular block.

Conner and Holt[4] analyzed 287 patients with coronary thrombosis. Approximately 85 per cent of these cases occurred in men and 15 per cent in women. One hundred and fifty-one of these patients had one or more electrocardiograms taken. Those individuals who did not show heart-block did better than those with heart-block. The authors found a mortality of 16.2 per cent in the whole group at the time of the first attack. They said in particular that patients with evidence of arborization or bundle-branch block did poorly.

White and Bland[5] in their study of the prognosis of 500 cases of angina pectoris and of 200 cases of coronary thrombosis, found an average duration of life of 4.4 years after the onset of the disease in 213 fatal cases of angina pectoris, and 1.5 years after the onset in 101 fatal cases of coronary thrombosis. They said, "The electrocardiogram was of little help in predicting the outcome, although a 'coronary' type of T-wave in Lead I or II was seen more often in the patients who died early. . . . The electrocardiogram did not help appreciably in this series." This last statement concerned the prognosis of coronary thrombosis.

Graybiel and Sprague,[6] who made an analysis of 395 cases of bundle-branch block, concluded:

"From the standpoint of diagnosis and prognosis it is important to determine its presence in cardiac patients.

"Bundle-branch block almost invariably indicates serious organic disease of the heart, usually coronary disease; the average duration of life of the 223 fatal cases in this series after the discovery of the conduction fault was one year and two months, but 85 other cases are still alive after an average of two years and eleven months following the discovery of the bundle-branch block.

"Partial bundle-branch block must be regarded clinically as equally significant with complete bundle-branch block, the prognosis in both being essentially the same."

Graybiel and White[7] in a study of 72 cases of complete auriculoventricular block, not yet published, have found that the average age at the time of discovery of the block was fifty-three years, the average duration of life after this discovery in 41 cases that died of heart disease was two years and two months and in 8 patients who died of other causes was six years and eight months and that the average duration of life to date in 17 living patients is six years and eleven months, a more favorable prognosis therefore than in the cases of bundle-branch block reported by Graybiel and Sprague.* Among the

*Six of the 72 patients of the series of Graybiel and White have not yet been heard from in the follow-up study.

72 cases of complete heart-block, 9 had angina pectoris without clinical coronary thrombosis, 4 had coronary thrombosis without angina pectoris, and 3 had both.

PRESENT STUDY

THE INCIDENCE OF HEART-BLOCK AMONG PATIENTS SHOWING CLINICAL EVIDENCE OF CORONARY DISEASE

Among 4,274 cases with signs or symptoms of cardiovascular disease in which electrocardiograms were made and which make up the total number of cases analyzed in the present study, 1,028, or 24 per cent, showed clinical evidence of coronary disease, namely, paroxysmal angina pectoris or coronary thrombosis, or both, in the following proportion: paroxysmal angina pectoris alone, 700 cases or 68+ per cent; coronary thrombosis alone, 169 cases or 16+ per cent; paroxysmal angina pectoris and coronary thrombosis, 159 cases or 15+ per cent.

TABLE I

TOTAL CASES OF CORONARY DISEASE DIAGNOSED CLINICALLY AND BY ELECTROCARDIOGRAPH (PAROXYSMAL ANGINA PECTORIS OR CORONARY THROMBOSIS)

Paroxysmal angina pectoris alone			700		
Coronary thrombosis alone			169		
Paroxysmal angina pectoris and coronary thrombosis			159		
				1,028	
Auriculoventricular or intraventricular block			105		
Both auriculoventricular and intraventricular block			5	110	10.7+%
Auriculoventricular block, total cases				25	2.4+%
Complete	5	0.4+%			
Partial	16	1.6–%			
Transient (partial)	4	0.4–%			
Intraventricular block, total cases				85	8.2+%
Lesser degrees	35	3.4+%			
Left bundle-branch block	40	3.9–%			
Right bundle-branch block	10	0.9–%			

Total cases of coronary disease diagnosed clinically equaled 24% of total of series of cardiovascular cases electrocardiographed (4,274)

A. *Group With Angina Pectoris.*

TABLE II

PAROXYSMAL ANGINA PECTORIS WITHOUT CORONARY THROMBOSIS (CLINICAL DIAGNOSIS)			700	
Auriculoventricular or intraventricular block			62	8.8 %
Both			3	0.4 %
Auriculoventricular block, total cases			11	1.5 %
Complete	1	0.1+%		
Partial	9	1.2+%		
Transient (partial)	1	0.1+%		
Intraventricular block, total cases			54	7.7 %
Lesser degrees	21	3.0 %		
Left bundle-branch block	27	3.8+%		
Right bundle-branch block	6	0.8+%		

TABLE III

PAROXYSMAL ANGINA PECTORIS, ALL CASES			859	
Auriculoventricular or intraventricular block			78	9.1–%
Both			3	0.3+%
Auriculoventricular block, total cases			13	1.5+%
Complete	2	0.2+%		
Partial	10	1.1+%		
Transient (partial)	1	0.1+%		
Intraventricular block, total cases			68	7.9 %
Lesser degrees	26	3.0+%		
Left bundle-branch block	35	4.0+%		
Right bundle-branch block	7	0.8+%		

B. *Group With Coronary Thrombosis.*

TABLE IV

CORONARY THROMBOSIS (CLINICAL DIAGNOSIS), ALL CASES			328	
Auriculoventricular block or intraventricular block			43	13.1+%
Both			2	0.6+%
Auriculoventricular block, total cases			14	4.2+%
Complete	4	1.2+%		
Partial	8	2.4+%		
Transient (partial)	2	0.6+%		
Intraventricular block, total cases			31	9.5 %
Lesser degrees	12	3.7–%		
Left bundle-branch block	14	4.3–%		
Right bundle-branch block	5	1.5+%		

TABLE V

CORONARY THROMBOSIS (CLINICAL DIAGNOSIS) WITHOUT PAROXYSMAL ANGINA PECTORIS			169	
Auriculoventricular or intraventricular block			27	15.9+%
Both			2	1.1+%
Auriculoventricular block, total cases			12	7.1–%
Complete	3	1.7+%		
Partial	7	4.1+%		
Transient (partial)	2	1.2 %		
Intraventricular block, total cases			17	10.0 %
Lesser degrees	7	4.1+%		
Left bundle-branch block	6	3.5+%		
Right bundle-branch block	4	2.3+%		

THE INCIDENCE OF CLINICAL EVIDENCE OF CORONARY DISEASE AMONG CASES SHOWING HEART-BLOCK

We shall now analyze the cases of heart-block found in the total group of patients with cardiovascular symptoms or signs (4,274) of whom electrocardiograms were made with respect to clinical manifestations of coronary disease.

TABLE VI

TOTAL CASES OF HEART-BLOCK	274	
Auriculoventricular block, total cases	117	
Intraventricular block, total cases	181	
Auriculoventricular and intraventricular block, total cases	24	
Coronary disease evident clinically	110	40+%
Paroxysmal angina pectoris alone	65	23.7 %
Paroxysmal angina pectoris, total cases	81	29.5+%
Coronary thrombosis, total cases	45	16.4+%
Coronary thrombosis alone	29	10.5+%
Paroxysmal angina pectoris and coronary thrombosis	16	5.8 %

Total cases of heart-block equaled 6.4 per cent of the total of series of cardiovascular cases electrocardiographed (4,274).

Among the 24, or 20.5+ per cent, of the 117 patients with auriculoventricular block who showed at the same time intraventricular block, only 5 belonged to the group in which the block was related to clinical evidence of coronary disease. The proportion was as follows: 2 patients with partial auriculoventricular block combined with intraventricular block (lesser degrees) had paroxysmal angina pectoris alone; 1 patient with partial auriculoventricular block combined with intraventricular block (lesser degree) had coronary thrombosis alone; 1 patient with partial auriculoventricular block combined with intraventricular block (left bundle-branch block) had paroxysmal angina pectoris alone; and, finally, the fifth patient, showing complete auriculoventricular block combined with intraventricular block (right bundle-branch block), had coronary thrombosis alone.

A. *Group With Auriculoventricular Block.*

TABLE VII

	COMPLETE	PARTIAL	TRANSIENT		TOTAL	
			COMPLETE	PARTIAL		
Total cases of auriculoventricular block	22	86	2	7	117	
Clinical evidence of coronary disease, total cases	5	16	0	4	25	21.3+%
Paroxysmal angina pectoris alone	1	9	0	1	11	9.4+%
Paroxysmal angina pectoris total	2	10	0	1	13	11.1+%
Coronary thrombosis total	4	8	0	2	14	11.9+%
Coronary thrombosis alone	3	7	0	2	12	10.2+%
Paroxysmal angina pectoris and coronary thrombosis	1	1	0	0	2	1.7+%
Intraventricular block, total cases					24	20.5+%

Total cases of auriculoventricular block equaled 2.4 per cent of total of series of cardiovascular cases electrocardiographed (4,274).

B. *Group With Intraventricular Block of All Degrees.*

TABLE VIII

TOTAL CASES OF INTRAVENTRICULAR BLOCK			181	
Lesser degrees	85			
Left bundle-branch block	77			
Right bundle-branch block	19			
Clinical evidence of coronary disease, total cases			85	46.9+%
Paroxysmal angina pectoris alone	54	29.8+%		
Paroxysmal angina pectoris total	68	37.5+%		
Coronary thrombosis total	31	17.1+%		
Coronary thrombosis alone	17	9.3+%		
Paroxysmal angina pectoris and coronary thrombosis	14	7.7+%		
Auriculoventricular block			24	13.3+%
Complete	4	2.2+%		
Partial	20	11.0+%		
Transient	0			

Total cases of intraventricular block equaled 4.2 per cent of total of series of cardiovascular cases electrocardiographed (4,274).

C. *Left Bundle-Branch Block.*

TABLE IX

TOTAL CASES OF LEFT BUNDLE-BRANCH BLOCK			77	
Coronary disease evident clinically, total cases			41	53.2 %
Paroxysmal angina pectoris alone	27	35.0+%		
Paroxysmal angina pectoris total	35	45.4+%		
Coronary thrombosis total	14	18.1+%		
Coronary thrombosis alone	6	7.7+%		
Paroxysmal angina pectoris and coronary thrombosis	8	10.3+%		
Auriculoventricular block			4	5.1+%
Complete	1	1.2+%		
Partial	3	3.8+%		
Transient	0			

Total cases of left bundle-branch block equaled 1.8 per cent of total of series of cardiovascular cases electrocardiographed (4,274).

D. *Right Bundle-Branch Block.*

TABLE X

TOTAL CASES OF RIGHT BUNDLE-BRANCH BLOCK			19	
Coronary disease evident clinically, total cases			11	57.8+%
Paroxysmal angina pectoris alone	6	31.5+%		
Paroxysmal angina pectoris total	7	36.7+%		
Coronary thrombosis total	5	26.3+%		
Coronary thrombosis alone	4	21.0+%		
Paroxysmal angina pectoris and coronary thrombosis	1	5.2+%		
Auriculoventricular block			2	10.5 %
Complete	1	5.2+%		
Partial	1	5.2+%		
Transient	0			

Total of cases of right bundle-branch block equaled 0.4 per cent of total of series of cardiovascular cases electrocardiographed (4,274).

We would interpolate at this point, with especial regard to prognosis, data concerning a number of the patients with auriculoventricular heart-block, whose etiological factors, so far as clinical evidence goes, are other than coronary disease.

TABLE XI

ETIOLOGICAL FACTORS OTHER THAN EVIDENT OR PROBABLE CORONARY DISEASE RESPONSIBLE FOR AURICULOVENTRICULAR BLOCK

TOTAL CASES OF AURICULOVENTRICULAR BLOCK	117	
Acute or subacute rheumatic infection (among 63 cases)	6	5.1 %
Cardiovascular syphilis (among 81 cases; 1 other case had intraventricular block)	1	0.08%
Congenital heart-block	3	2.5 %
Digitalis intoxication (among 41 cases)	9	8.5 %
Diphtheria (among 4 cases)	2	1.6 %
Leaving a balance of cases of coronary disease or of unknown etiology	96	

Among the 4,274 cases in which electrocardiograms were made, there were, as noted in the table, 41 cases with manifestations of digitalis intoxication but only 9 of these showed auriculoventricular block. We can feel reasonably certain that digitalis given to a few of the patients with coronary thrombosis was not responsible for the infrequent heart-block among such patients. Among these same 4,274 patients, 81 had cardiovascular syphilis, and only 1 of these showed auriculoventricular block; 63 had acute or subacute rheumatic infection, and only 6 of these showed auriculoventricular block; 4 had diphtheria, and 2 of these showed auriculoventricular block, and finally, 3 cases showed congenital heart-block. Only one of the 81 cases of syphilis showed intraventricular block. Digitalis was apparently not responsible for intraventricular block in any of our cases, nor was rheumatic infection. The group with diphtheria was too small to be of any significance.

THE PROGNOSIS OF THE CASES OF HEART-BLOCK ACCORDING TO THE PRESENCE OR ABSENCE OF CLINICAL EVIDENCE OF CORONARY DISEASE

With relation to the prognosis in the patients who have shown heart-block, we have made a division into two groups, namely, those with and those without clinical evidence of coronary disease; it is necessary to subdivide them further as follows: (a) patients alive at last report in whom we cannot foretell the probable duration of life; and (b) patients who are known to have died. In nearly every instance in this latter group death was due to the heart disease.

A. *Prognosis of Cases of Auriculoventricular Block.*—Of the 25 patients with auriculoventricular block with angina pectoris or coronary thrombosis or both, nine were alive at last report. Our records show duration of life according to age after the discovery of heart-

block until the last report as follows: four patients, between 50 and 60 years of age have lived 8, 3, 0.8, and 0.03 years, respectively; three patients, between 60 and 70 years of age, have lived 4, 2, and 0.75 years, respectively; and two patients over 70 years old have lived 3, and 0.08 years, respectively.

The remaining 16 of the 25 patients with auriculoventricular block with angina pectoris or coronary thrombosis or both have died.* Their duration of life according to age after the discovery of heart-block was as follows: five patients under 50 years of age lived 10, 2, 1, 1, and 0.16 years, respectively; five between 50 and 60 years of age lived 2, 1, 0.66, 0.16, and 0.03 years, respectively; four patients between 60 and 70 years of age lived 1, 0.25, 0.16, and 0.003 years, respectively; and two patients over 70 years old lived 9 and 1 years, respectively.

Of the 92 patients with auriculoventricular block without either paroxysmal angina pectoris or coronary thrombosis, 26 of those followed up were alive at the last report. Our records show the duration of life according to age after the discovery of heart-block until last report, as follows: seven patients under 50 years of age have lived 10, 5, 1, 0.75, 0.66, 0.5, and 0.4 years, respectively; six patients between 50 and 60 years of age have lived 17, 6, 1, 1, 0.16, and 0.03 years, respectively; ten patients between 60 and 70 years old have lived 11, 8, 3, 2, 2, 2, 2, 1, 0.33, 0.08 years, respectively; and three patients over 70 years old have lived 3, 0.16, and 0.08 years, respectively. To the group of living patients belong sixteen additional patients not followed up and fifteen patients with auriculoventricular block due to digitalis intoxication or other factors previously mentioned.

The remaining 35 of the 92 patients with auriculoventricular block without angina pectoris or coronary thrombosis have died.† Their duration of life according to age after the discovery of block was as follows: four patients under 50 years of age lived 2, 0.83, 0.25, and 0.08 years, respectively; four patients between 50 and 60 years old lived 6, 3, 1, and 1 years, respectively; seven patients between 60 and 70 years old lived 2, 2, 2, 1, 0.25, 0.047, and 0.021 years, respectively; and sixteen patients over 70 years old lived 4, 2, 1, 1, 0.9, 0.83, 0.75, 0.41, 0.33, 0.25, 0.16, 0.16, 0.08, 0.02, 0.02, 0.003 years, respectively. To the above must be added four patients who showed auriculoventricular block due to various other factors previously mentioned, and which cases we have not taken into present account so far as prognosis is concerned.

*Six of these patients died suddenly (two in recognized attacks of angina pectoris); eight died of congestive failure (one in acute pulmonary edema); and two died apparently in Adams-Stokes attacks.

†Seven of these patients died suddenly; eight died of congestive failure (one in acute pulmonary edema); four died in Adams-Stokes attacks, ten with noncardiac lesions, and six of unknown causes.

Summarizing the above described groups, we find the average age at, and average duration of life after, the discovery of auriculoventricular block as follows:

Patients (25) who have shown auriculoventricular block with paroxysmal angina pectoris or coronary thrombosis or both: nine were alive at the last report, average duration of life, after discovery of block 29.3 months, average age 61.4 years; sixteen died, average duration of life after discovery of block 22.4 months, average age 55.2 years. Patients (57) who have shown auriculoventricular block without either paroxysmal angina pectoris or coronary thrombosis and without other known etiological factors: twenty-six were alive at the last report, average duration of life after discovery of block 41.2 months, average age 48.8 years; thirty-one have died, average duration of life after discovery of block 13 months, average age 60 years.

B. *Prognosis of Cases of Intraventricular Block.*—Of the 85 patients with intraventricular block with paroxysmal angina pectoris or coronary thrombosis or both, 31 were alive at last report. Our records show the duration of life according to age after discovery of the block until last report in the cases followed up as follows: two patients under 50 years old have lived 8 and 3 years, respectively; nine patients between 50 and 60 years of age have lived 8, 5, 3, 3, 1, 1, 0.5, 0.4, and 0.01 years, respectively; eight patients between 60 and 70 years old have lived 3, 3, 2, 1, 1, 1, 0.66, and 0.33 years, respectively; and four patients over 70 years old have lived 5, 1, 0.5, and 0.02 years, respectively. Eight patients were not followed up.

Fifty-four of the 85 patients with intraventricular block with angina pectoris or coronary thrombosis are known to have died.* Their duration of life according to age after the discovery of the block was as follows: two patients under 50 years of age lived 2 and 0.16 years, respectively; twenty-two patients between 50 and 60 years old lived 5, 5; 3, 2, 2, 1, 1, 1, 1, 1, 1, 1, 0.83, 0.75, 0.5, 0.41, 0.41, 0.33, 0.25, 0.16, 0.08, and 0.003 years, respectively; twenty-two patients between 60 and 70 years old lived 11, 8, 6, 5, 4, 3, 3, 2, 2, 1, 0.66, 0.58, 0.41, 0.33, 0.33, 0.33, 0.33, 0.26, 0.25, 0.25, 0.07, and 0.02 years, respectively; and eight patients over 70 years old lived 1, 1, 1, 0.66, 0.5, 0.33, 0.25, and 0.08 years, respectively.

Of the 96 patients of intraventricular block without paroxysmal angina pectoris or coronary thrombosis and without other known etiological factors 54, including 16 patients not followed up, belong to the group alive at the last report, and our records show duration of life according to age after the discovery of block until last report as follows: four patients under fifty years of age have lived 5, 0.75,

*Thirty-seven of these patients died suddenly (several in recognized attacks of angina pectoris), and twelve others are known to have died with congestive failure (two in acute pulmonary edema).

0.58, and 0.16 years, respectively; nine patients between 50 and 60 years old have lived 8, 5, 3, 3, 0.5, 0.5, 0.33, 0.05, and 0.03 years, respectively; fifteen patients between 60 and 70 years old have lived 11, 9, 5, 4, 3, 3, 2, 2, 2, 2, 1, 0.5, 0.5, 0.08, and 0.05 years, respectively; and ten patients over 70 years old have lived 6, 5, 3, 3, 3, 1, 0.16, 0.08, 0.06, and 0.04 years, respectively. The other 42 patients are known to have died;* their duration of life according to age after the discovery of block was as follows: five patients under 50 years of age lived 3, 2, 2, 0.66, and 0.25 years, respectively; thirteen patients between 50 and 60 years old lived 9, 5, 3, 2, 1, 1, 1, 0.66, 0.5, 0.33, 0.16, 0.08, and 0.05 years, respectively; eleven patients between 60 and 70 years old lived 3, 2, 2, 2, 2, 1, 1, 1, 1, 0.41, and 0.16 years, respectively; and thirteen patients over 70 years old lived 6, 3, 2, 1, 1, 1, 0.83, 0.75, 0.66, 0.33, 0.25, 0.16, and 0.06 years, respectively.

Summarizing the data on the above described groups of intraventricular block, we find an average duration of life as follows:

Of patients (85) who have shown intraventricular block with paroxysmal angina pectoris or coronary thrombosis or both: 23 patients followed up were alive at the last report, average duration of life after the discovery of block 27 months, average age 61 years; 54 patients died, average duration of life after discovery of the block 18 months, average age 60.7 years; the remaining 8 patients were not followed up. Of patients (96) who have shown intraventricular block without paroxysmal angina pectoris or coronary thrombosis and without other known etiological factors: 54 patients were alive at the last report, average duration of life after discovery of block 29 months, average age, 62 years; 42 patients died, average duration of life after discovery of block 18.8 months, average age† 61.1 years.

SUMMARY AND CONCLUSIONS

Our attention has been drawn during the past year to the fact that, contrary to one's first expectation and to general impressions, there is a marked discrepancy between the occurrence of auriculoventricular and intraventricular block and the clinical evidence of coronary disease, namely, angina pectoris and gross myocardial infarction. Therefore, we have determined the relative incidence of concurrence of auriculoventricular and intraventricular block, as shown by electrocardiography, and of angina pectoris and of coronary thrombosis in a large series of patients with cardiovascular symptoms or signs carefully studied by ourselves during the past fifteen years.

*Ten of these patients are known to have died suddenly; fifteen died in congestive failure (one in an attack of cardiac asthma), one died during an attack of coronary thrombosis, and one in an Adams-Stokes attack.

†The average age is based on the cases with known ages, and not on the total number of cases, as there are missing records in a few instances.

We have found that only 8.8 per cent of 700 patients with angina pectoris uncomplicated by clinical coronary thrombosis showed heart-block, either auriculoventricular block (1.1 per cent) or intraventricular block (7.3 per cent), or both (0.4 per cent), and that only 13.1 per cent of 328 cases of coronary thrombosis, with or without angina pectoris, showed heart-block, either auriculoventricular block (3.6 per cent) or intraventricular block (8.9 per cent) or both (0.6 per cent).

Conversely, of 117 patients with auriculoventricular block in the series, only 9.4 per cent had angina pectoris without clinical coronary thrombosis, and only 11.9 per cent more had clinical evidence of coronary thrombosis with or without angina pectoris, making a grand total of 21.3 per cent of cases of auriculoventricular block with clear evidence of coronary disease.

Finally, of 181 cases of intraventricular block of all grades, including 77 cases of full left bundle-branch block and 19 cases of full right bundle-branch block, 29.8 per cent showed angina pectoris without clinical coronary thrombosis, and only 9.3 per cent showed coronary thrombosis with or without angina pectoris, making a grand total of 46.9 per cent of cases of intraventricular block with clear evidence of coronary disease. Details as to the relationship of left and right bundle-branch block to clinical manifestations of coronary disease have been presented; in both groups a few over half had angina pectoris, coronary thrombosis, or both.

It is evident that coronary disease or other pathogenesis responsible for heart-block, either auriculoventricular or intraventricular, does not run parallel to gross lesions of the larger arterial stems of the coronary circulation, the obstruction of which produces clinical evidence of coronary disease in the form of myocardial infarction. Of special interest is the fact that intraventricular block was relatively almost as common in cases of angina pectoris without clinical coronary thrombosis (except perhaps as a terminal event) as in cases of clinical coronary thrombosis without angina pectoris. On the other hand the association of auriculoventricular and intraventricular block with coronary disease is frequent enough to be highly significant.

Furthermore, in our series the prognosis of older patients (over fifty years old) of heart-block, either auriculoventricular or intraventricular, is about equally unfavorable whether or not there are associated clinical evidences of coronary disease, that is, angina pectoris and coronary thrombosis.

In the instance of the sixteen patients with auriculoventricular block with angina pectoris or coronary thrombosis who died, the average age at the time of the discovery of the block was fifty-five years

and the average duration of life after the discovery of the block was twenty-two months, while the thirty-one patients with fatal auriculoventricular block without angina pectoris or coronary thrombosis recognized clinically, or other known etiological factors, averaged sixty years of age at the time of the discovery of the block and survived such discovery an average of thirteen months.

In the instance of the 54 patients with intraventricular (bundle-branch) block with angina pectoris or coronary thrombosis who died, the average age at the time of the discovery of the block was sixty-one years and the average duration of life thereafter eighteen months, while the 42 patients with fatal intraventricular (bundle-branch) block without angina pectoris or coronary thrombosis recognized clinically averaged sixty-one years of age at the time of the discovery of the block and survived such discovery nineteen months. There are a few individuals who survive many years and to old age with auriculoventricular or intraventricular block.

It may be concluded from this analysis that the coronary supply to the auriculoventricular node and bundle and its branches is not necessarily blocked as a result of the lesion (thrombosis or embolism) which blocks the coronary supply to the areas of the heart (anterior apical and posterior basal portions of the left ventricular myocardium) most commonly affected in clinical coronary thrombosis, but that such supply may be seriously involved by atherosclerotic or other processes with poor prognosis even when there is no associated angina pectoris or clinical evidence of sudden blockage of the anterior descending branch of the left coronary artery or of the main trunk of the right.

REFERENCES

1. Wolff, L., Parkinson, J., and White, P. D.: An Undescribed Cardiac Mechanism: "Intraventricular Block" With Short P-R Interval in Healthy Young People Prone to Paroxysmal Tachycardia, J. Clin. Investigation **9**: 28, 1930.
   Idem: Bundle-Branch Block With Short P-R Interval in Healthy Young People Prone to Paroxysmal Tachycardia, AM. HEART J. **5**: 685, 1930.
2. Holzmann, M., and Scherf, D.: Ueber Elektrokardiogramme mit verkürzter Vorhof-Kammer-Distanz und positiven P-Zacken, Ztschr. f. klin. Med. **121**: 404, 1932.
3. Levine, S. A.: Coronary Thrombosis: Its Various Clinical Features, Medicine **8**: 245, 1929.
4. Conner, L. A., and Holt, E.: The Subsequent Course and Prognosis in Coronary Thrombosis, An Analysis of 287 Cases, AM. HEART J. **5**: 705, 1930.
5. White, P. D., and Bland, E. F.: A Further Report on the Prognosis of Angina Pectoris and of Coronary Thrombosis: A Study of Five Hundred Cases of the Former Condition and of Two Hundred Cases of the Latter, AM. HEART J. **7**: 1, 1931.
6. Graybiel, A., and Sprague, H. B.: Bundle-Branch Block: Analysis of Three Hundred and Ninety-Five Cases, Am. J. M. Sc. **185**: 395, 1933.
7. Graybiel, A., and White, P. D.: An Analysis of Seventy-Two Cases of Complete Auriculoventricular Heart-Block, With Especial Reference to Prognosis. (In preparation.)

THE USE OF ETHER IN MEASURING THE CIRCULATION TIME FROM THE ANTECUBITAL VEINS TO THE PULMONARY CAPILLARIES*

WILLIAM M. HITZIG, M.D.†
NEW YORK, N. Y.

DURING the past decade the circulation time in man has been studied intensively. Discussions of methods employed in these studies may be found in papers by Kisch,[1] Blumgart,[2] Tarr, Oppenheimer, and Sager,[3] and others. Essentially, all circulation-time methods consist of the introduction of a foreign substance into a peripheral systemic vein and the measurement of the time interval elapsing between the injection and the arrival of the fastest flowing particle at designated points in the circulation.

The signal reactions in such methods are either subjective or objective, depending upon the physical and pharmacological characteristics of the substance injected. Methods employing physical properties of substances as end points (fluorescein, sodium chloride, and radium emanation) are mainly objective, whereas methods using substances that evoke a specific pharmacological or physiological response are either subjective (calcium chloride, sodium dehydrocholate, and saccharin), or objective (carbon dioxide, histamine, and sodium cyanide). These methods have wide clinical applicability, but they present certain limitations since, with the exceptions of radium emanation and sodium cyanide, they fail to give more than indirect information as to the velocity of blood flow in component portions of the pathway traversed by the injected substance.

By the application of the radium emanation and sodium cyanide methods, attempts have been made in the past to study the blood velocity in selected segments of the circulation. Blumgart and Weiss[4] introduced radium emanation into a peripheral vein and with the aid of a detector determined its arrival at designated points in the pathway, measuring thereby the speed of flow in the peripheral (''arm to right heart'' time) and pulmonary (''right heart to arm'' time) circulation. Robb and Weiss[5] similarly employed small doses of sodium cyanide to obtain values for the ''peripheral venous'' segment, and for the ''crude pulmonary time.'' Valuable as these methods are, they measure arbitrary rather then physiological segments of the circulation.

Until recently, no method had been described which permits the differentiation of the right and left heart circuits on a physiological or

*From the Medical Services and the Laboratories of The Mount Sinai Hospital.
†Eugene Meyer, Jr., Fellow in Pathology.

dynamic basis. At a meeting of the Society for Experimental Biology and Medicine held April 18, 1934, the author[6] described the ether method as an objective as well as a subjective method clinically applicable for measuring the circulation time of the pathway of the right heart unit. By the application of this method, the two sides of the heart with their respective afferent and efferent vessels may be studied as functional subdivisions of the vascular pathway which includes the pulmonary circuit.

The principle of the method consists of the intravenous introduction of a volatile substance and the measurement of the time that elapses before the odor characteristic of the injected substance is perceived by either patient or investigator. During this time interval the foreign substance passes through the peripheral venous segment, the right heart, and the pulmonary artery to the pulmonary arterial capillaries whence it volatilizes into the pulmonary alveoli. It then ascends with great rapidity through the air passages to the olfactory organ and is readily recognized. Among the volatile substances available for measuring the circulation time from the antecubital veins to the pulmonary capillaries, the author has found ether to be highly satisfactory, for the following reasons:

1. Its volatility at blood temperature is so great (ether boils at about 35° C.) that even when a small quantity is injected, the amount that volatilizes in the pulmonary capillaries during the first circuit of the blood is invariably sufficient to be perceptible by smell.
2. Only a small volume is needed. This permits rapid intravenous introduction so that the ether will flow in a small blood volume. The advantage of this is that it results in a sharp definition, not only of the time of injection, but also of the time of arrival in the pulmonary capillaries.
3. It gives no constitutional symptoms in the quantities used. In over 350 patients, some of whom had two and even three injections, no untoward systemic reactions were encountered. In a few instances, ether injections seemed to have a transient "beneficial" effect upon the circulation. This was occasionally observed in the patient with decompensated heart disease who stated that his "heart felt better" or that he "could breathe more easily" following the injection.
4. Because of its marked volatility, the measurement can be repeated as often as desired.
5. Paravenous infiltration causes no necrosis.

Although ether has certain definite advantages, it is still not the ideal substance. During its injection, the subject may be aware of a "creeping" sensation along the course of the vein. In about one-third of the patients, particularly in those whose circulation time is either near the upper limit of normal, or delayed, or in those whose antecubital veins are small, pain of a transient cramplike character may appear immediately following the injection. This may last a few moments, but it

rarely lasts over a minute unless the procedure is complicated by paravenous infiltration. In sensitive individuals as determined by the Libman[7] test, the pain appears to be of higher incidence and greater severity. Although it is usually confined to the site of injection, it frequently radiates along the course of the vein to the shoulder, and at times may conceivably be due to venous spasm rather than direct venous injury. A change in structure of the vein as determined by palpation may occur at the site of injection. This may vary from simple localized thickening to local thrombosis. In a series of 110 patients in whom the veins were carefully observed for a period of at least seven days, localized changes in the vein (thickening or thrombosis) occurred twenty-nine times, or in about 26 per cent of the cases. Except for the local change, this complication has never produced any untoward symptoms. In fact, one is usually unaware of its existence since it develops slowly and causes no pain, unless there has been paravenous infiltration. Pulmonary embolism has never been observed. Should a change take place in the structure of a vein, it is usually clinically recognizable from three to seven days after the injection. Its delayed appearance suggests a low grade chemical endophlebitis which incidentally may occur during the administration of other related volatile substances. For example, Vorzimer[8] obtained a high incidence of venous thrombosis following the use of acetone for circulation time studies. In his series, similar pathological changes in the veins also became manifest at the local site between the third and seventh day.

I. MATERIAL AND METHODS

A study was made of 352 individuals between the ages of sixteen and seventy-five years. Of this group, 272 were ward patients* suffering from various conditions, 52 were ambulant patients from the out-patient department, and 28 were normal young adults between the ages of fifteen and twenty-three years. In 164 there was no evidence of any circulatory disturbance, whereas in a group of 87 patients, the circulatory manifestations of either left or right or universal (left and right) heart failure were present.

The ether circulation time from the antecubital veins was determined in the entire group. In 8 patients it was also measured from the dorsal ankle veins. The saccharin circulation time and the venous pressure were measured in 158 patients of the series.

A. *The Measurement of the Circulation Time With Ether.*—The ether circulation time from an antecubital vein is determined by the following method: 5 minims (0.33 c.c.) of ether and 5 minims of normal saline are drawn into a 1 or 2 c.c. syringe to which a 20-gauge needle is attached. The mixture separates out into layers. The individual reclines in bed

*These patients were studied on the Medical Services of Dr. George Baehr and Dr. B. S. Oppenheimer, and on the Surgical Service of Dr. Harold Neuhof.

comfortably from about fifteen to twenty minutes. His arm is propped up to a level corresponding to the right auricle. He is familiarized at first with the odor of ether. He is then instructed to relax, breathe normally, and to announce when he smells the ether. It is advisable to forewarn the subject that he may experience momentary discomfort at the site of the venipuncture during the period of injection. A tourniquet is then applied, and the needle is inserted into a large antecubital vein. After waiting about a minute following the release of the tourniquet to allow local circulatory disturbances to subside, the investigator rapidly injects the mixture, taking only a fraction of a second for the procedure. The end point is sharp and unmistakable. Moreover, an observer in a position close to the subject can perceive the ether odor almost as rapidly as the patient. This objective confirmation, valuable as it is in itself, becomes of especial importance when studying unconscious or uncooperative patients. The time interval that elapses between the injection of ether and the registration of the end point is clocked with a stop watch and represents the circulation time of the pathway of the right heart unit. To yield results which will check closely on repetition, the subject must relax and must not hold his breath during the procedure, for this retards the venous return to the heart.

The ether circulation time from a dorsal ankle vein is determined in the same manner. The individual lies in the recumbent position. The chosen vein is raised to the level of the right auricle. The veins being of small caliber in this location, a hypodermic rather than a larger needle is preferable for the injection.

B. *The Measurement of the Circulation Time With Saccharin.*—For purposes of comparison with the ether circulation time, and for the derivation of the circulation time of the pathway of the left heart unit, the saccharin method of Fishberg, Hitzig, and King[9] was employed in a group of 158 patients. The procedure is essentially the same as that for the ether method. The end point, however, is a sweet taste at the back or tip of the tongue. In health, the saccharin circulation time ("arm to tongue" time) varies from 9 to 16 seconds. The sodium dehydrocholate (decholin) method of Winternitz, Deutsch, and Bruell,[10] recently studied by Tarr, Oppenheimer and Sager[2] was also employed in 8 normal patients of this series. The saccharin and decholin readings agreed very closely (within 1 to 2.5 seconds).

In a number of the cases studied earlier, delayed local thrombosis developed more frequently following the simultaneous or consecutive injections of ether and saccharin into the same vein at the same sitting. This also occurred in two of the patients who received decholin-ether injections. The incidence of this complication may be considerably lessened by employing separate veins for the injections when saccharin or decholin is used in conjunction with ether.

C. *The Measurement of the Venous Pressure.*—The venous pressure was determined by a slight modification[11] of the direct method of Taylor, Thomas, and Schleiter.[12] Normal measurements with this method vary between 4 and 8 cm. of blood. Readings were of value in selected cases in determining the presence or absence of circulatory disturbances and in corroborating the clinical impressions of either left or right heart failure.

Except for general implications, the correlation of the venous pressure with the ether and saccharin circulation times will not be presented in this paper. A later publication on the venous pressure by Dr. Arthur M. Fishberg and the author will include such a study.

II. NORMAL CIRCULATION TIME VALUES

A. *The Normal (Ether) Circulation Time From the Antecubital Veins to the Pulmonary Capillaries. Measure of the Right Heart Unit (Arm-to-Lung Time).*—In 164 "normal" subjects in whom there were no manifest circulatory disturbances, the ether circulation times were distributed as shown in Table I.

TABLE I

"ETHER TIME" FROM ANTECUBITAL VEINS TO PULMONARY CAPILLARIES

CIRCULATION TIME (SEC.)	NUMBER OF INDIVIDUALS
3.5-3.75	9
4.0-4.75	40
5.0-5.75	39
6.0-6.75	42
7.0-7.75	23
8.00	11
Total	164

The end point was definite in practically every case, only an occasional measurement requiring repetition. Repeated injections in a series of 22 patients agreed either exactly or within from 0.5 to 2 seconds. Readings of 8.5 to 9.5 seconds were occasionally obtained when the end point was recorded only subjectively. After reexamination of these patients objectively to exclude local olfactory disturbances, the circulation times usually fell below 8 seconds.

The mean ether circulation time derived from the data in Table I is 5 54 seconds and the standard deviation is 1.25 seconds. As commonly interpreted by statisticians this would mean that 95 per cent of all normal cases will show a circulation time of from over 3 to 8 seconds or that more than two-thirds of all normal cases will show a circulation time between 4.3 and 6.8 seconds. The range actually varied from 3.5 to 8 seconds.

An analysis of our normal series reveals no apparent relationship between the "ether time" and the age, sex, or venous and arterial pres-

sures. Similarly, no correlation can be established between the ether time and the slight fluctuations in pulse rate which varied in our patients during the period of examination from 70 to 96 beats per minute. In 5 children between the ages of seven and eleven years, not included in the above series, the ether time was faster, ranging between 2.5 and 5.5 seconds.

The quantity and physical state of the injected ether evidently bear important relationships to the accuracy of the ether circulation time. A relationship of the amount of injected ether to the ether time was recognized following the separate introduction of 0.33 c.c. and 0.15 c.c. of ether into a group of 8 patients and comparing results. In each instance, not only was the end point with the smaller dose less defined, but the circulation time showed a prolongation of from 1.5 to 3 seconds. The delay as well as the lessened acuity of the end point were even more marked when 0.15 c.c. of ether was dissolved in 3 c.c. of saline and injected into the same group of 8 patients. The prolongation of the circulation time in the latter instance may be attributed, first, to an increased volume which requires a longer injection time; second, to the use of dissolved ether which apparently volatilizes less completely and less readily in the pulmonary capillaries than ether not in solution; and third, to the lower pressure gradient of the ether in the alveoli when smaller quantities of the substance are employed.

To prove that the pressure gradient of ether in the pulmonary bed is adequate when 0.33 c.c. (5 minims) of ether is employed, this quantity (0.33 c.c.) and double this quantity (0.66 c.c.) were injected separately into a group of five patients and the results compared. Although the end point was sharper following the larger dose, the ether time was not significantly accelerated.

TABLE II

COMPARISON OF ETHER TIMES OBTAINED WITH 0.33 C.C. AND 0.66 C.C. OF ETHER

CASE NO.	ETHER TIME (0.33 C.C.) SEC.	ETHER TIME (0.66 C.C.) SEC.
1	6.0	5.0
2	4.5	4.5
3	7.0	6.0
4	7.5	6.0
5	5.0	4.5

A quantitative relationship between rate of respiration and the ether time undoubtedly exists. Such a relationship was also found by Fishberg, Hitzig, and King in their saccharin studies. Rapid breathing will hasten the venous return to the right heart and thereby accelerate the circulation time, whereas slow breathing will retard the venous return and prolong the circulation time. In a small group of patients whose "ether times" were near the upper limit of normal (6 to 8 seconds),

rapid breathing (40 per minute) caused an acceleration of blood flow of 1 to 2.5 seconds, whereas in patients with "ether times" of 4 to 6 seconds, the acceleration, if present, did not exceed 0.5 to 1.5 seconds.

Strictly speaking, the ether time includes not only the time which elapses during the passage of ether from the antecubital veins to the pulmonary capillaries, but also the interval required for its flow through the tracheobronchial system to the nose. However, because of the rapidity with which a light gas diffuses in a gaseous mixture, it may be assumed that the time required for the ether to flow from the pulmonary alveoli to the nasopharynx is negligible in comparison with the actual circulation time. Hence, for practical purposes, the pulmonary arterial capillaries may be regarded as the site of the ether end point.

The question arises whether the phase of the respiratory cycle during which the injected ether is discharged into the lungs affects the circulation time. The speed of passage of ether from the alveoli to the olfactory organ will depend primarily on the pressure gradient of ether at the pulmonary bed. If this pressure gradient is assumed to be adequate, the modifying factors involved consist of the to-and-fro movements of air during inspiration and expiration. From a theoretical consideration of the law of diffusion of gases and of the normal velocity of air during the two phases of the respiratory cycle, it is clear that the diffusion of ether will offset to a varying extent any retardation due to inspiration or any acceleration due to expiration.

B. *The Comparison of the Normal Ether to the Normal Saccharin Circulation Time.*—Of particular interest is the comparison of the ether time, which is a measure of the circulation time from the antecubital veins to the arterial capillaries of the lung, with the "saccharin time," which determines the speed of the circulation from the antecubital veins through the lungs to the capillaries of the tongue. In a consecutive group of fifty-two normal subjects the percentage relationship of ether time to saccharin time showed the following variations:

TABLE III

PERCENTAGE RELATIONSHIP OF NORMAL ETHER TIME TO NORMAL SACCHARIN TIME

ETHER TIME EXPRESSED AS % SACCHARIN TIME	NUMBER OF INDIVIDUALS
33-39	6
40-49	32
50-59	12
60-66	2

This study shows that in 44 (84 per cent) of the 52 normal patients, the ether time was from 40 to 59 per cent of the saccharin time. In 32 individuals (61 per cent) the ether time was from 40 to 49 per cent of the saccharin time. A comparison of the extreme limits of normal ether time (3.5 to 8 sec.) with those of normal saccharin time (9 to

16 sec.) shows a 39 per cent relationship existing at the lower limit of normal and a 50 per cent relationship at the upper limit of normal.

C. *The Normal Circulation Time From the Pulmonary Capillaries to the Capillaries of the Tongue as Measured by the Saccharin Time–"Ether Time" Difference. Measure of Left Heart Unit (Lung-to-Tongue Time).*—By subtracting the ether time which is a measure of the right heart unit, from the saccharin time which measures the circulation time from the antecubital veins to the lingual capillaries, the circulation time of the left heart unit, i.e., from the pulmonary capillaries to the capillaries of the tongue, may be obtained. This may be designated as the saccharin time–ether time difference. Although the difference between the maximum saccharin time (16 sec.) and the maximum ether time (8 sec.) is 8 seconds, the saccharin time–ether time difference in the fifty-two normal subjects varied between 4.5 and 9.5 seconds. Consequently, one may conclude that in a normal individual the maximum time required for a foreign substance to pass from the capillaries of the lung to the capillaries of the tongue or to traverse the pathway of the left heart unit will usually not exceed 9.5 seconds. Such a maximum difference was recorded in only four individuals of the normal series. This quantitative relationship of the ether time to the saccharin time, that is to say, the saccharin time–ether time difference, becomes of particular importance in the study of patients with circulatory disturbances.

D. *The Normal Ether Circulation Time From the Dorsal Ankle Vein to the Pulmonary Capillaries.*—The circulation time from the dorsal ankle vein to the pulmonary capillaries was recorded in eight normal patients. The end point was sharp in every case. The series is, however, too small to allow conclusions as to the limits of normal.

TABLE IV

ETHER TIME FROM ANTICUBITAL AND DORSAL ANKLE VEINS TO PULMONARY CAPILLARIES

CASE NO.	FROM ANTECUBITAL VEIN (SEC.)	FROM DORSAL ANKLE VEIN (SEC.)
1	8	18
2	6	24
3	5	30
4	7	23
5	6	20
6	7	34
7	6	30
8	5	16

In this group the ether time varied from 16 to 34 seconds. Many factors probably affect the circulation time from the lower extremity, namely, the age and height of the individual, the tortuosity of the veins of the lower limb, and the intraabdominal pressure.

Because of wide fluctuations of the normal ether circulation time from the dorsal ankle veins, this procedure has limited application. Com-

parative determinations from both lower limbs may be of value, however, in cases of unilateral edema or venous obstruction. This is well illustrated by observations in the following case.

Case.—A fifty-year-old female, following a febrile illness, developed massive enlargement of her left lower extremity six months before she came under our observation. With the exception of the tense pitting edema which extended upward to the inguinal region, she was in good physical condition. The differential diagnosis rested between venous and lymphatic obstruction.

The ether circulation times from the ankle veins of both limbs and the venous pressures in both femoral veins were determined above the area of edema (4 cm. below the inguinal ligament). The results are given in Table V.

TABLE V

LOWER EXTREMITY	ETHER TIME (ANKLE) (SEC.)	VENOUS PRESSURE (FEMORAL) (CM. OF BLOOD)
Right	17.5	6.0
Left	34.0	20.5+*

*Blood clotted in manometer at this level.

A comparison of the ether times and venous pressures shows conclusively the presence of venous obstruction above the left femoral vein probably due to an old thrombophlebitis of either the left common or the left external iliac vessel. Coexisting lymphatic obstruction, however, could not be excluded.

III. CIRCULATION TIMES IN HEART FAILURE

A. *Failure of the Left Side of the Heart.*—The subject of circulation times in failure of the left side of the heart was noted by Hitzig[6] and has been discussed at length by Hitzig, King, and Fishberg.[13] Their study reveals that in most instances of left ventricular failure, whether due to hypertensive, arteriosclerotic, syphilitic, or rheumatic heart disease, the ether time may be within normal limits, but the saccharin time may be much prolonged. The resulting abnormal increase of the saccharin time–ether time difference suggests that the retardation of blood velocity in such instances is localized to the pathway of the left heart unit or to that portion of the arm-to-tongue circulation which is beyond the pulmonary arterial capillaries (lung-to-tongue segment). The normal systemic venous pressure and the normal ether time testify unequivocally to the functional efficiency of the right ventricle. In other cases, however, even though the venous pressure remains within normal limits, the ether time may be moderately prolonged, occasionally to 14 seconds. This may occur particularly when the left ventricular insufficiency is severe and the pulmonary engorgement pronounced. The abnormal ether and saccharin times point to retardation of blood velocity

in both the arterial and venous portions of the pulmonary circuit. As a rule, the saccharin time–ether time differences in such instances also show disproportionate prolongation indicating that in these cases the rate of pulmonary blood flow is also predominantly slowed in the segment beyond the pulmonary arterial capillaries. The prolongation of the ether time in left ventricular failure may really be regarded as a manifestation of "incipient" failure of the right side of the heart. It reveals that although the right ventricle is able to maintain a normal systemic venous pressure, it is unable, laboring as it is against an increased pulmonary resistance (hypertension of pulmonary circuit), to maintain the normal blood velocity through its circulatory pathway. As has been mentioned by Hitzig, King, and Fishberg, normal circulation times are occasionally encountered in left ventricular failure. This was also recently observed in a case of malignant hypertension in which the venous pressure was 6 cm. of blood, the ether time was 6.5 seconds and the saccharin time was 13.5 seconds.

B. *Failure of the Right Side of the Heart.*—When the general venous pressure is elevated because of intrinsic functional or organic disease of the heart, the ether circulation time, except in occasional cases, is prolonged. Such prolongation appears to be proportional to the degree of myocardial insufficiency, or roughly to the height of the venous pressure. The ether times in eighteen cases of frank right heart failure which were of rheumatic, syphilitic, and arteriosclerotic etiology varied from 9 to 27 seconds. The saccharin times were correspondingly or disproportionately prolonged. The saccharin time–ether time differences were either within normal limits or slightly or markedly increased. They ranged from 9 seconds (upper limit of normal) to as high as 32 seconds. The variation in the lung-to-tongue time appears to be related to the degree of pulmonary congestion. Of interest in this regard are two cases with contrasting clinical pictures which exhibit the above extremes in the saccharin time–ether time difference. The circulatory disturbance in one case suggested at first the possibility of primary right heart failure. The venous pressure was 26 cm. of blood; the ether time was 17 seconds, the saccharin time was 26 seconds; and the saccharin time–ether time difference was 9 seconds. This patient had marked cyanosis, no dyspnea in bed, very little, if any, orthopnea, and no clinical signs of pulmonary engorgement. There was peripheral edema, but no hydrothorax. Post-mortem examination revealed extensive coronary artery disease with recent thrombosis of the right posterior descending branch and myomalacia of the posterior wall of the left ventricle and septum. In the second patient, who also suffered from severe coronary artery disease with recent thrombosis, the extreme slowing of pulmonary blood flow which occurs most strikingly in association with failure of the left ventricle was well illustrated by the following measurements. The venous pressure was 22 cm., the ether time was 26 seconds; the saccharin time was 58 sec-

onds; and the saccharin time–ether time difference was 32 seconds. Clinically, he was acutely ill, cyanotic, dyspneic, and orthopneic at rest, and he presented signs of marked pulmonary engorgement. He had bilateral hydrothorax for which he was tapped on several occasions. At post-mortem examination severe coronary artery disease, recent thrombosis of the left circumflex and right coronary arteries, and myomalacia of both ventricles were found. Ascites was also present. From these clinical, circulatory, and anatomical observations it may be said that although in each case both ventricles were functionally incapacitated due to the same disease process, the dynamic disturbance was chiefly right-sided heart failure in the first case, and predominantly left-sided heart failure in the second case. Since both patients had almost identical venous pressures, it is interesting to correlate the clinical pictures with the enormous variations in the lung-to-tongue time. Since the lung-to-tongue time appears to be a rough index of the extent of congestion in the venous segment of the pulmonary circuit, the absence of hydrothorax in the first patient and its occurrence in the second patient suggest a possible relationship between the genesis of this condition and the degree of prolongation of the saccharin time–ether time difference.

True cases of "isolated" primary right heart failure were not observed.

C. *Heart-Block.*—Four patients with heart-block and accompanying bradycardia were studied. In one patient with partial heart-block and a pulse rate of 45, the ether and the saccharin times were within normal limits. In another patient with complete block and a bradycardia of 32, the lung-to-tongue time, as manifested by a saccharin time–ether time difference of 17.5 seconds, was considerably slowed. The ether time and the saccharin time were 7.5 and 25 seconds, respectively.

In two cases of complete heart-block with bradycardias which fluctuated between 28 and 35, both the ether time and the saccharin time were abnormally delayed. Despite the presence of normal venous pressures and compensatory arterial pressures (systolic hypertension and high pulse pressure), the ether times were 10.5 and 12.5 seconds and the saccharin times were respectively 29 and 32 seconds. In both of these cases, the high saccharin time–ether time differences indicated disproportionate prolongation of the lung-to-tongue time. The retardation of pulmonary blood flow in these cases may be attributed not only to the left ventricular insufficiency but also to the profound slowing of the heartbeat.

IV. CIRCULATION TIMES IN INTRATHORACIC DISEASES

A. *Mediastinal Tumor With Superior Vena Cava Syndrome.*—In two patients suffering from mediastinal tumor with local elevation of the venous pressure, the ether time was high normal (7.5 and 8 sec.),

whereas in a third patient it was slightly retarded (10 sec.). Readings obtained with saccharin showed corresponding alterations of the saccharin time, but the saccharin time-ether time difference was within normal limits in all three cases. Observations with saccharin alone were made by Fishberg, Hitzig and King[14] in a fourth patient who presented a classical superior vena cava syndrome due to mediastinal Hodgkins disease. Despite an elevation of the venous pressure to about 32 cm., the saccharin time was 14 seconds from one antecubital vein and 18 seconds from a corresponding vein on the other arm.

Although the velocity of blood flow in the peripheral venous segment is probably retarded by a mediastinal tumor which causes stasis in the large systemic veins, the ether time may still remain within normal limits. As previously stated, the ether time in patients with right heart failure is usually prolonged to a degree which parallels the elevation of the systemic venous pressure. With a venous pressure elevation in right heart failure comparable to that usually obtained in mediastinal tumor, the circulation times with ether and saccharin would be considerably retarded. This observation indicates that the slowing of the ether circulation time occurs most markedly when the circulatory disturbance involves the entire pathway rather than only the peripheral venous segment of the right heart unit.

B. *Pleuropulmonary Diseases.*—The ether and saccharin circulation times were determined in a large group of patients who suffered from a variety of diseases involving the lungs and pleurae. The diseases studied included pneumonia, pleurisy with effusion, bronchial asthma, bronchiectasis, and pulmonary tuberculosis. The determinations were within the limits of normal except in occasional patients in whom the clinical picture was complicated by myocardial insufficiency and an elevated venous pressure.

C. *Unilateral Functioning Lungs.*—It is common knowledge among clinicians that the circulatory dynamics are only rarely disturbed in pulmonary conditions with single functioning lungs. This fact is substantiated objectively by circulation time studies which reveal conclusively that in such cases the velocity of blood flow through the lungs is almost never retarded. For example, in two cases of unilateral tension pneumothorax, in which there was moderate cyanosis and slight elevation of the venous pressure due probably to compression of the mediastinal veins, the ether and saccharin times were normal. Normal circulation times and venous pressures were recorded in four patients with massive unilateral pleural effusions of the idiopathic type despite the moderate shifting of the mediastinum to the unaffected side. Normal circulatory measurements were also obtained in a case of obstruction of the main bronchus with massive unilateral atelectasis, despite the presence of a moderate degree of cyanosis.

Circulatory studies were also carried out in conjunction with Dr. Harold Neuhof in eight patients with extensive unilateral disease of the lungs.

TABLE VI

CASE NO.	PULSE (PER MIN.)	RESPIRATION (PER MIN.)	VENOUS PRESSURE (CM.)	ETHER TIME (SEC.)	SACCHARIN TIME (SEC.)
1	96	22	4.0	2.75	
2	88	20	3.5	3.00	7.0
3	92	20	5.0	3.00	7.5
4	98	18	4.5	4.00	8.5
5	86	22	4.0	3.50	
6	88	20	5.5	4.00	10.0
7	94	20	3.5	3.00	
8	100	20	4.0	4.00	8.5

Although one lung was functionally eliminated by disease or operation or both, the venous pressures in this series ranged between 3.5 and 5.5 cm. and the ether times fell between 2.75 and 4 seconds. The saccharin times in five of these patients varied between 7 and 10 seconds. Three of these patients showed a faint degree of labial cyanosis. The above findings may be indicative of an accelerated pulmonary blood flow which may result from mechanisms compensating for the diminished aerating surface of the lungs.

IV. CIRCULATION TIMES IN BLOOD DISEASES

A. *Polycythemia.*—In two patients suffering from uncomplicated polycythemia vera, the ether time and the saccharin time were proportionately prolonged. In a third patient the circulation times were normal. The venous pressures were normal in all cases.

TABLE VII

CASE NO.	CIRCULATION TIMES IN POLYCYTHEMIA VERA	
	ETHER TIME	SACCHARIN TIME
1	11.5	21
2	12.0	22
3	7.5	16

B. *Anemia.*—The ether times in five cases of secondary anemia were between 3.5 and 4.5 seconds while the saccharin times varied between 8 and 11.5 seconds. In one case of pernicious anemia, the ether time was 6.5 seconds and the saccharin time was 14 seconds.

V. THYROID DISEASE

A. *Graves' Disease.*—This subject has been studied extensively by Blumgart and by Tarr, Oppenheimer and Sager. In a series of six patients observed by the author, the ether circulation times ranged between 3 and 4.5 seconds, whereas the saccharin times varied between 7 and 9.5 seconds.

B. *Postoperative Hypothyroidism.*—Cases of true myxedema were not observed. However, in three patients whose basal metabolic rates following subtotal thyroidectomy fluctuated between minus 20 and minus 30 per cent, ether times ranging between 7 and 8.5 seconds were obtained. The saccharin times were also near the upper limit of normal.

VI. MISCELLANEOUS CONDITIONS

Normal ether circulation times were also obtained in a variety of other clinical conditions in which there was no evidence of any coexisting circulatory disturbance. These included acute and chronic nephritis, nephroses, and cirrhosis of the liver.

COMMENT

The ether time, which measures the speed of blood flow from the antecubital veins to the pulmonary capillaries, serves as an index of the functional capacity of the right heart. Similarly the saccharin time–ether time difference determines the functional capacity of the left heart. With the exception of polycythemia vera in which there may also be universal retardation of the velocity of blood flow, the ether time appears to be normal in all noncardiac conditions that have been studied. Elevation of the venous pressure in the large systemic veins, unless caused by functional insufficiency of the right ventricle, is rarely accompanied by a significant prolongation of the ether time. This impression is based upon the findings in cases of mediastinal tumor and tension pneumothorax. Another interesting observation on this point was made in a patient who had unilateral elevation of the venous pressure (21 cm.) due probably to axillary or subclavian vein thrombosis with suspected partial recanalization. The ether time in that arm was 7.5 seconds. In the opposite arm where a venous pressure of 7 cm. was obtained, the ether time was 5.5 seconds. This shows that although there was a retardation of 2 seconds as compared with the sound side, the ether time on the abnormal side was still within the normal range.

Prolongation of the ether time and of the saccharin time–ether time difference occurs not only in frank right heart failure but also in left ventricular failure when the functional capacity of the right ventricle becomes insufficient to master the increased resistance in the pulmonary circuit. Although in these cases the prolonged ether time offers the only evidence of insufficiency of the right ventricle, this circulatory derangement is indicative of incipient failure of the right heart despite the presence of a normal venous pressure. There are also occasional cases of frank right heart failure secondary to antecedent left ventricular failure, in which the saccharin time–ether time difference may remain within the normal range, even though the ether and saccharin times are retarded. These findings are compatible with the well known clin-

ical concept, recently emphasized by Fishberg,[15] that the pulmonary congestion associated with left ventricular failure may often be considerably lessened upon the advent of right heart failure.

The comparative study of the ether and saccharin times in various types of heart failure is of value in localizing the portion of the circulation in which blood flow is retarded. By the combined application of these methods, evidence has also been obtained which offers convincing support to the "backward failure" theory of heart failure. At the suggestion of Dr. Ernst Boas, interesting observations in this regard were recently made in a case of essential hypertension with progressively developing heart failure. When first seen, this patient presented the classical syndrome of left ventricular failure. The venous pressure was 7 cm. of blood, the ether time was 7 seconds, and the saccharin time was 23 seconds. Two weeks later the venous pressure was essentially unchanged, but the ether time was 9 seconds and the saccharin time was 28 seconds. Gradually, within a period of three weeks thereafter, the usual phenomena of right heart failure became manifest. The venous pressure rose to 17 cm. of blood; the ether time was 16 seconds; and the saccharin time was 30 seconds. After a period of bed rest, digitalization, and diuresis, the venous pressure fell to 9 cm. of blood; the ether time was 8 seconds; and the saccharin time was 20 seconds. The measurements repeated prior to discharge, two weeks later, showed a venous pressure of 6.5 cm. of blood, an ether time of 7.5 seconds, and a saccharin time of 18 seconds.

SUMMARY

1. Ether introduced intravenously may be used as a subjective and objective method for the determination of the circulation time from the antecubital veins to the pulmonary capillaries (arm-to-lung time). The ether time serves as a measure of the functional capacity of the right heart unit.

2. A study was made of 352 individuals. In 164 "normal" adults, the ether time from the antecubital veins varied between 3.5 and 8 seconds. The ether time from the dorsal ankle veins in 8 adult individuals ranged between 16 and 34 seconds.

3. The percentage relationship of ether time to saccharin time ranged from 33 to 66 per cent in 52 normal individuals.

4. The saccharin time–ether time difference, which is an indirect measure of the circulation time from the pulmonary arterial capillaries to the capillaries of the tongue (lung-to-tongue time), may serve as an index of the functional capacity of the left heart unit. The range in 52 normal subjects was 4.5 to 9.5 seconds.

5. Prolongation of ether time usually occurred in right heart failure, in certain instances of left heart failure with incipient right heart failure, in heart-block, and in polycythemia vera.

6. The ether time in three cases of mediastinal tumor with compression of superior vena cava was either high normal or only slight retarded, despite the elevation of the venous pressure in the large systemic veins.

7. In all other clinical conditions uncomplicated by insufficiency of the right heart, the ether time was usually within normal limits.

8. Ether and saccharin circulation times in conditions associated with unilateral functioning lungs are either extremely rapid or within the lower limits of normal. The accelerated pulmonary blood flow may be an expression of mechanisms operating to compensate for the diminished aerating surface of the lungs.

9. A comparison of the ether and saccharin time is of value in localizing the segment of the circulation in which blood flow is retarded.

10. Evidence obtained by the ether and saccharin methods supports the "backward failure" theory of heart failure.

REFERENCES

1. Kisch, B.: Handbuch der normalen und pathologischen Physiologie, vol. VII, pt. 2, p. 1205, 1927, A. Bethe u. G. von Bergmann.
2. Blumgart, H. L.: The Velocity of Blood Flow in Health and Disease: The Velocity of Blood Flow in Man and Its Relationship to Other Measurements of the Circulation, Medicine **10**: 1, 1931.
3. Tarr, L., Oppenheimer, B. S., and Sager, R. V.: The Circulation Time in Various Clinical Conditions Determined by the Use of Sodium Dehydrocholate, AM. HEART J. **8**: 766, 1933.
4. Blumgart, H. L., and Weiss, S.: Studies on the Velocity of Blood Flow. VII. The Pulmonary Circulation Time in Normal Resting Individuals, J. Clin. Investigation **4**: 399, 1927.
5. Robb, G. P., and Weiss, S.: A Method for the Measurement of the Velocity of the Pulmonary and Peripheral Venous Blood Flow in Man, AM. HEART J. **8**: 650, 1933.
6. Hitzig, W. M.: Measurement of the Circulation Time from the Antecubital Veins to the Pulmonary Capillaries, Proc. Soc. Exper. Biol. & Med. **31**: 935, 1934.
7. Libman, E.: Observations on Sensitiveness to Pain, Tr. A. Am. Physicians **41**: 305, 1926.
8. Vorzimer, J.: Personal communication.
9. Fishberg, A. M., Hitzig, W. M., and King, F. H.: Measurement of the Circulation Time with Saccharin, Proc. Soc. Exper. Biol. & Med. **30**: 651, 1933.
10. Winternitz, M., Deutsch, J., and Bruell, Z.: Eine Klinische brauchbare Bestimmungsmethode der Blutumlaufszeit mittels Decholininjektion, Med. Klin. **27**: 986, 1931; ibid. **28**: 831, 1932.
11. Fishberg, A. M., Hitzig, W. M., and King, F. H.: The Dynamics of Myocardial Infarction, Arch. Int. Med. **54**: 997, 1934.
12. Taylor, F. A., Thomas, A. B., and Schleiter, H. G.: Direct Method for Estimation of Venous Blood Pressure, Proc. Soc. Exper. Biol. & Med. **27**: 867, 1930.
13. Hitzig, W. M., King, F. H., and Fishberg, A. M.: Circulation Times in Failure of the Left Side of the Heart, Arch. Int. Med. **55**: 112, 1935.
14. Fishberg, A. M., Hitzig, W. M., and King, F. H.: Unpublished.
15. Fishberg, A. M.: On Orthopnea, Libman Anniv. Volumes **1**: 415, 1932.

Department of Clinical Reports

A CASE OF PULSATING SPLEEN IN MITRAL AND TRICUSPID DISEASE*

DON C. SUTTON, M.D., AND VANCE RAWSON, M.D.
CHICAGO, ILL.

MANGES[1] was the first to report a case of pulsating spleen in mitral and tricuspid disease. Except for the following case, no instance of pulsation of the spleen has been observed in the large number of cases seen in the Cardiac Follow-up Clinic of Cook County Hospital.

An Italian girl, seventeen years of age, was referred to the cardiac clinic on March 31, 1931, following her discharge from the hospital. The only serious illness in her past history was scarlet fever in 1927; however, in February, 1931, dyspnea, edema and precordial pain were noticed. A month later, at her first visit to the clinic, she was observed to be a well-nourished girl, with normal temperature, but with a regular tachycardia of 120 per minute.

Inspection revealed a diffuse apex impulse in the anterior axillary region, accompanied by a systolic retraction. Neither cyanosis nor edema was present. A distinct presystolic thrill was easily felt over the precordium, in addition to the shock due to closure of the pulmonic valves.

Percussion, confirmed by a teleroentgenogram, gave the outline seen in Fig. 1. The heart area extended 12 cm. to the left of the midline and 6 cm. to the right, with a cardiothoracic ratio of 0.70. Systolic, presystolic, and middiastolic mitral murmurs were heard, as were the usual moist râles in the bases of the lungs. A positive Wassermann reaction was interpreted as being due to a congenital syphilis. At this time neither the liver nor the spleen was palpable.

Her condition improved until August, 1931, when an auricular fibrillation was first observed. In May, 1932, she was referred to the hospital because of congestive heart failure, at which time only the liver was palpable. On her return to the clinic, three months later, she was found to have developed a tricuspid insufficiency, as evidenced by the enlarged, pulsating liver, and positive venous pulsation in the veins of the neck. At the same time there was felt a large spleen, extending to the crest of the ileum, with definite expansile pulsation. Other clinicians in attendance have confirmed these observations.

At present her condition is unaltered, her blood pressure as heretofore being 120 mm. systolic and 70 mm. diastolic. The pulsations of both liver and spleen have shown no change since August, 1932. Following the oral administration of hippuran, the outlines of the kidneys, liver, and spleen were plainly visible, as verified by Dr. Roger Vaughn, who interpreted the x-ray pictures. Simultaneous tracings of the hepatic and splenic pulsations were recorded upon the electrocardiogram, Lead II. The pulsations recorded in the spleen are unquestionably simultaneous

*From the Cardiac Follow-up Clinic at Cook County Hospital.

with those of the liver. The illustration (Fig. 1) is a photograph of the outlines of the heart, the liver, and the spleen. The cardiac outline is the result of superimposing the 2 meter cardiac shadow upon the chest.

DISCUSSION

According to Manges,[1] Nicholas Tulpius, of Amsterdam, in 1652 reported the first observation of pulsation of the spleen. Gerhardt, in 1882, reported three cases, all in patients with aortic insufficiency. In two, the splenic pulsation was observed during attacks of lead colic, the pulsations disappearing with recovery from the colic. In the third case, pulsation was coincident with the development of pericarditis. In 1887, Prior reported two cases, one in a patient with aortic insufficiency, the splenic pulsation appearing during an attack

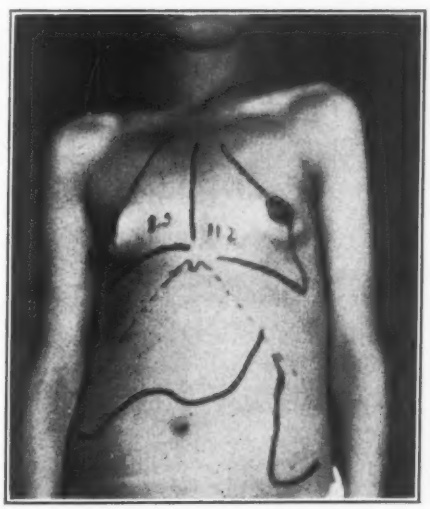

Fig. 1.—Showing the outline of the heart traced on the chest from the last 2 meter heart plate. The liver and spleen were palpated and outlined as shown.

of typhoid fever. The second patient had a marked dilatation of the left ventricle, and the pulsating spleen was noted during the course of a croupous pneumonia. Drasche, in 1888, observed pulsation of the spleen during an attack of pneumonia in a patient with aortic insufficiency. Sailer[2] observed pulsation of the spleen in a patient with aortic insufficiency, during the course of a terminal bacterial endocarditis.

There have been, therefore, nine instances of the observation of this condition, six of which were reported between the years of 1882 and 1888. Manges says that he looked for a second case for the next six years, and we have kept it in mind during the past three years, but thus far we have not encountered a second case. All the cases reported, except that of Manges, who found a pulsating spleen in mitral

and tricuspid disease, have been observed in the presence of aortic insufficiency. Our patient has never shown any evidence of aortic insufficiency. In the light of the cases reported thus far, there would appear to be four possible explanations for such a condition:

1. In aortic insufficiency there is probably a direct transmission of pulsations to the arteries of the spleen.

2. Transmission of the pulsations from the pulsating liver. Mechanically, the impulse produced in the vena cava by tricuspid insufficiency would have to pass through the capillaries of the liver into the portal veins and then into the splenic vein. This appears to us to be improbable, as it does also to the anatomists whom we have consulted. Nevertheless, such an explanation cannot be entirely disregarded.

3. That there is an anomalous communication between the splenic vein and the inferior vena cava. Such a communication with the vena cava would permit of the direct transmission of the impulse to the splenic vein, as it is transmitted to the hepatic vein in liver pulsation. Shepherd[3] reports that there is a specimen in the museum at McGill University in which there is a large anastomosis between the renal and splenic veins.

4. An arteriovenous communication involving the splenic vein. When one considers the anatomy of the venous sinuses of the spleen this would appear to be the only possible explanation.

Unfortunately, so far as is known, none of the cases reported came to autopsy. However, the extreme rarity of pulsating spleen makes it probable that it can be due only to one of the latter anomalies. In our opinion the most likely cause of a pulsating spleen in mitral disease and an intact aortic valve is the presence of an anomalous communication between the splenic vein and the vena cava.

SUMMARY

A case of pulsation of the spleen in mitral and tricuspid disease is reported, supplementing the single case thus far reported (by Manges). Eight cases of pulsating spleen occurring in aortic insufficiency have been reported by others.

REFERENCES

1. Manges, Morris: Pulsating Spleen in Mitral and Tricuspid Disease, Am. J. M. Sc. **154**: 72, 1917.
2. Sailer, Joseph: Pulsating Spleen in Aortic Insufficiency, AM. HEART J. 3: 447, 1928.
3. Shepherd, Francis J.: Anomalies of the Veins, Reference Handbook of Medical Science, Vol. 8, p. 206, New York, 1908, William Wood & Company.

Society Transactions

AMERICAN HEART ASSOCIATION, 1935

The eleventh annual scientific session of the American Heart Association was held on June 11, 1935, at the Hotel Claridge, Atlantic City, N. J., with Dr. John Wyckoff as presiding officer. The following program was presented.

Program

The Duration of Life Following Initial Attack of Heart Failure. J. Murray Steele, M.D., New York, N. Y.

ABSTRACT

A numerical survey of cardiac patients admitted to the Hospital of the Rockefeller Institute for Medical Research between January, 1920, and December, 1932, is presented. Only those individuals, 154 in number, who suffered at some time from symptoms of heart failure at rest and whose records continued until death or up to January, 1935, were included in the study.

Of the 154 patients, 66 suffered from heart disease of rheumatic origin, 61 of arteriosclerotic and hypertensive origin, 9 of syphilitic origin, and 18 of unknown origin. The more clearly defined differences in behavior between the larger groups (rheumatic and arteriosclerotic) may be briefly pointed out. Duration of life as well as ability to work after the first attack of heart failure was longer in the individuals whose disease was rheumatic in nature (3.2 and 1.5 years, respectively) than in those whose difficulty was dependent upon arteriosclerosis or hypertension (2.6 and 1.1 years, respectively). It appeared also that the individuals in both groups whose auricles were fibrillating survived for a considerably longer period of time (3.5 years) than did those whose rhythm was normal (1.8 years). The difference in duration of life in the two groups may be due in part to the fact that the rheumatic group was much younger (36.7 years each) than the arteriosclerotic (59.3 years), and in part to the fact that the proportion of cases of auricular fibrillation was much greater in the rheumatic group (3:1) than in the arteriosclerotic (1:1).

In the whole group of 154 patients the average duration of life from the onset of the first attack of heart failure was 2.9 years. The yearly decrease in the number of patients alive following the first attack was found to be proportional to the number of living patients, approximately one-fourth dying each year. Three-fourths of the original group of patients sustained a second attack of heart failure at rest. It is of especial interest that the yearly decrease in number of patients living following a second attack of heart failure was also a logarithmic curve and that approximately the same proportion, one-fourth of the surviving patients, died each year. The suggestion is, naturally, that heart failure, unless fatal, does not alter to any great extent the subsequent length of life. The group of patients who suffer at least two attacks of heart failure are also interesting because they comprise that large class often labelled "chronic cardiac" which presents complex problems in treatment and its evaluation and serves generally as material for comparison of new and special methods of treatment with the usual forms of medical care—rest, restriction of fluids, and the administration of diuretics and digitalis.

The Results of Treatment in Cardiovascular Syphilis. Paul Padget, M.D., and Joseph Earle Moore, M.D., Baltimore, Md. See page 1017.

The Significance of Electrocardiographic Changes in Diphtheria. E. A. Burkhardt, M.D., Cary Eggleston, M.D., and Lawrence Smith, M.D., New York, N. Y.

ABSTRACT

This study concerns the relation of the onset of the disease to the occurrence of manifest changes in the electrocardiogram. Alterations in conduction and in the form of the ventricular complexes are described; the effects of therapy and the clinical manifestations are discussed.

The Pathological Analysis of Diphtheritic Myocarditis With Especial Reference to Electrocardiographic Findings. Lawrence Smith, M.D., E. A. Burkhardt, M.D., and Cary Eggleston, M.D., New York, N. Y.

ABSTRACT

The pathological findings in one hundred fatal cases of diphtheria are described. In many cases there appears to be a rough parallelism between the degree of change of conductivity, as measured by the electrocardiograph, and the severity of the anatomical changes. The alterations noted in certain protracted cases suggest that diphtheritic myocarditis should be considered as a cause of secondary heart disease a little later in life.

Peripheral Venous Phenomena in Congestive Heart Failure. William J. Kerr, M.D., San Francisco, Calif.

ABSTRACT

In the presence of right heart failure the tricuspid valve becomes incompetent, the venous pressure is elevated, and the liver becomes obviously distended. Under these circumstances the positive jugular pulsation following contraction of the right ventricle is propagated widely and under suitable manipulation can be described in the veins of the forehead, arms, hands, and legs. It is a stasis wave which travels along a distended vein.

The Relationship of Blood Pressure, Peripheral Vasomotor Activity, and Environmental Temperature. Ashley W. Oughterson, M.D., New Haven, Conn.

ABSTRACT

In this study a variety of patients was observed under conditions of controlled temperature and humidity. Blood pressure readings were correlated with peripheral skin temperatures while influenced by different levels of environmental temperature and humidity. It was found that in some individuals with hypertension the blood pressure could be raised as much as 100 mm. Hg on changing environmental temperature and humidity. The elevation of blood pressure was accompanied by a peripheral vasoconstriction. Older patients with a less elastic vascular bed did not show such marked changes. Normal subjects also showed little or no response to changes in environmental temperature and humidity. These observations suggest that certain individuals are hypersensitive to changes in environmental temperature and humidity.

The Influence of the Heat Regulatory Mechanism on Raynaud's Disease. Herman E. Pearse, Jr., M.D., Rochester, N. Y. See page 1005.

Observations Upon Electrocardiographic Tracings Obtained by the Use of Esophageal Leads in the Human Subject. W. Hurst Brown, M.D., Baltimore, Md.

ABSTRACT

The method is described, and the curves obtained are contrasted with standard and chest leads. The characteristics of the curves of the auricular complex are analyzed in both health and disease. Examples of auricular extrasystoles, flutter and fibrillation, and of sinus standstill and heart-block are examined. Animal experiments designed to elucidate points of a fundamental character are briefly described. The indications for the use of esophageal leads are presented.

The Protective Effect of a Collateral Vascular Bed Upon Coronary Occlusion. Claude S. Beck, M.D., Cleveland, Ohio.

ABSTRACT

The epicardium was removed. The endothelial layer of the pericardium was roughened. The pericardium and pericardial fat became adherent. Bands of silver were placed around the major coronary arteries. These vessels were occluded, a little at a time, by successive operations. Almost the entire coronary tree was occluded with recovery of the dog. A capillary injection of myocardium was obtained through the collateral vascular bed thus established.

It would appear that the presence of a collateral vascular bed protects the heart from sudden occlusion of a major coronary artery. In this respect the operation will serve as a prophylaxis against the ravages of sudden coronary occlusion.

The Development of Mitral Stenosis in Young People With a Note on the Frequent Misinterpretation of a Middiastolic Murmur at the Cardiac Apex. E. F. Bland, M.D., Paul D. White, M.D., and T. D. Jones, M.D., Boston, Mass. See page 995.

Follow-up Study of Sixty-Four Patients With Right Bundle-Branch Conduction Defect. Francis Clark Wood, M.D., William A. Jeffers, M.D., and Charles C. Wolferth, M.D., Philadelphia, Pa. See page 1056.

The Effect of Irregular Cardiac Rhythms on the Minute Volume Output of Blood From the Heart in Human Beings. Harold J. Stewart, M.D., N. F. Crane, M.D., J. E. Dietrich, M.D., and W. P. Thompson, M.D., New York, N. Y.

ABSTRACT

Paroxysmal tachycardia, both when the auricles are beating regularly (supraventricular) and irregularly (auricular fibrillation), as well as the very slow cardiac rhythm of complete heart-block, may be associated with diminished minute volume output of blood from the heart in the resting individual. A fibrillating heart slowed by digitalis may be as effective a pump as is that same heart after reversion to normal rhythm, the heart still under the influence of digitalis.

The Normal Electrocardiogram in Two Hundred Individuals With Special Reference to the Chest Leads. William Hallaran, M.D., and R. A. Shipley, M.D., Cleveland, Ohio.

ABSTRACT

Electrocardiograms have been made on 100 men and 100 women between the ages of twenty and thirty-five years, all of whom had a negative history, negative cardiovascular examination, and normal blood pressure. The normal variations in duration, amplitude, and contour of the various complexes have been observed and recorded

in the three conventional leads and in a chest lead using the apex and left leg. Special attention has been paid to slurring of QRS and elevation or depression of S-T interval. In twenty-five cases the effect of varying the position of the precordial electrode, using this method of leading from the chest, has been studied. In forty cases, for comparison, the chest lead using the A-P position of the electrode has been employed. It has been found that: (1) the magnitude of the QRS and T-deflections in males falls within a higher range than in females; (2) there is no significant difference between the records obtained using as chest leads (a) the apex and the left leg and (b) the apex and the back; (3) variation in the position of the precordial electrode produces marked changes in the contour of the QRS complex but does not materially alter the T-wave.

The Clinical Value of the Fourth Lead, as Observed in 3000 Ambulatory Patients. Clayton J. Lundy, M.D., Lawrence L. McLellan, M.D., Charles M. Bacon, M.D., and Ray Merchant, M.D., Chicago, Ill.

ABSTRACT

Clinical and electrocardiographic data were studied in an attempt to determine the value of Lead IV. It was found that the fourth lead gave evidence which, either as confirmatory evidence or as an additional finding, was helpful in the diagnosis of all forms of heart disease. It added tangible proof of the presence of early rheumatic heart disease. In chronic arteriosclerotic heart disease the fourth lead was of independent diagnostic value in 20 per cent of the cases, and of confirmatory value in 40 per cent.

A Study of 150 Cases of Coronary Thrombosis Treated With Low Calorie Diets. Arthur M. Master, M.D., Harry L. Jaffe, M.D., and S. Dack, M.D., New York, N. Y.

ABSTRACT

In 150 cases of coronary thrombosis the treatment consisted of immediate and prolonged bed rest, an 800 calorie diet and morphine and codeine when necessary. The diminished food intake lowered the basal metabolism to minus 20 or minus 30, decreased the heart work, avoided gastrocardiac reflexes. It is believed that the low diet was responsible for the prompt disappearance of pain and for the favorable outcome of most of the cases. The mortality in the entire series was 13 per cent, in the case of first attacks, only 5.5 per cent. Sixty-seven and one-half per cent of the patients were able to return to work.

The following papers were read by title.

Observations on Cardiovascular Syphilis. Louis A. Kapp, M.D., New York, N. Y.

ABSTRACT

An analysis of a series of cases of cardiovascular syphilis is presented. The influence of various factors is discussed: (1) personal data (age, race, occupation, habits, etc.); (2) luetic infection (date of infection, Kahn or Wassermann reaction, other luetic manifestations, specific treatment); (3) other diseases or infections (hypertension, arteriosclerosis, focal infections, rheumatic fever, pulmonary tuberculosis, etc.).

The frequency, intensity, and onset of the outstanding signs and symptoms are stated. Laboratory findings are described. Subdivision is made into (a) simple aortitis, with or without widening of the aorta; (b) complicated aortitis with aortic insufficiency, hypertension, arteriosclerosis, etc., and (c) aortic aneurysm. Several unusual cases of aneurysm of the aorta—two with sudden death following

rupture of the aorta—are demonstrated. The effect of antiluetic therapy with special reference to cardiac insufficiency is discussed.

Acute Arterial Occlusion: Reestablishment of Adequate Circulation Through Collateral Arterial Pathways by Passive Vascular Exercises. L. G. Herrmann, M.D., Cincinnati, Ohio.

ABSTRACT

The author has utilized the principle of increasing the arterial circulation in an extremity by rhythmic changes in the environmental pressure. Eighteen patients with peripheral embolism or arterial thrombosis occurring as a complication of serious cardiovascular disease have been treated successfully by passive vascular exercises. A discussion of the pathological physiology of the peripheral circulation after sudden occlusion of a major artery is presented with evidence to show that this method offers a most efficient and practical means of overcoming, without strain or shock to the seriously ill cardiac patient, the circulatory disturbances which result from such sudden accidents.

The Etiology and Pathogenesis of Auriculoventricular Heart-Block: Report of Representative Cases With Detailed Histopathological Studies. Wallace M. Yater, M.D., Washington, D. C.

ABSTRACT

There appear to be three chief causes of this condition: calcification in the region of the A-V bundle, large gumma in the septum involving the bundle, and fibrotic interruption of the bundle or its branches. The first is usually the result of strain at the junction of the membranous and muscular portions of the septum or of calcification of the vegetations of subacute bacterial endocarditis. The third follows impairment of the vascularity of the conduction system. The blood supply of the conduction system is discussed. Representative cases are presented, with histological studies.

The Relationship of Heart-Block, Auriculoventricular and Intraventricular, to Clinical Manifestations of Coronary Disease, Angina Pectoris, and Coronary Thrombosis. Jorge Salcedo-Salgar, M.D., Bogota, Colombia, and Paul D. White, M.D., Boston, Mass. See page 1067.

Paroxysmal Tachycardia. John P. Anderson, M.D., Cleveland, Ohio.

ABSTRACT

Conclusions are based on a study of 100 patients with paroxysmal tachycardia observed over varying periods up to twelve years. It is considered to be a functional heart condition carrying little or no danger to life but causing a great deal of misery to those so afflicted. The effects of various methods of vagal stimulation are discussed, as well as the effects of absorption from focal infections. Therapy by drugs such as digitalis, quinidine, sedatives, stimulants, gland extracts, ergotamine, and mecholin is presented.

Factors Influencing the Intensity of the First Heart Sound. Alexander Margolies, M.D., and Charles C. Wolferth, M.D., Philadelphia, Pa.

ABSTRACT

This study is an attempt to analyze the various factors which may influence the intensity of the first heart sound: namely, age, sex, thickness of the chest wall, blood pressure, heart rate, heart size, the presence of heart disease and certain other

diseases, the conduction time (P-R interval), and electrocardiographic evidence of myocardial damage and myocardial infarction. Five hundred patients with regular sinus rhythm, normal conduction time, and single first heart sounds were used. Sex was without influence. Hypertension, thyrotoxicosis, tachycardia, and small heart size tended to increase the intensity. Increased age, bradycardia, apical systolic murmurs, cardiac enlargement and myocardial disease tended to diminish the intensity. The most influential single factor was the auriculoventricular conduction time as measured by the P-R interval. When the P-R interval was short (0.12 to 0.14 second), the sound tended to be loud; when the interval was long (0.18 to 0.21 second), the sound tended to be weak; intermediate P-R intervals (0.15 to 0.17 second) tended to be associated with sounds of medium intensity. Furthermore, the evidence suggested that most of the other factors were chiefly operative through their influence on the conduction time. The three exceptions were myocardial infarction and thickness of the chest wall which tended to diminish the intensity and mitral stenosis which increased it.

Electrocardiograms on 167 Healthy Infants and Children. Clough Turrill Burnett, M.D., and Evelyn Laura Taylor, A.B., Denver, Colo. To be published in AM. HEART J.

The Orthodiagram in the Diagnosis and Treatment of Heart Disease. Chester M. Kurtz, M.D., Madison, Wis.

ABSTRACT

By the method of Eyster and Hodges 2,000 orthodiagrams have been made in 1,350 cases. An extensive follow-up study has been carried out with the same technic. Certain conclusions are drawn as to characteristic change in the shape of the heart in the presence of various valve lesions. It is also shown that by using the prediction formulas of Eyster and Hodges, the normal range is extremely narrow and relatively small degrees of enlargement can be detected with fair accuracy. The importance of certain physical signs in determining cardiac enlargement is demonstrated.

The Effect of Ouabain Upon Electrocardiograms of Specific Muscle Lesions. J. S. Robb, M.D., M. S. Dooley, M.D., J. G. F. Hiss, M.D., and R. C. Robb, M.D., Syracuse, N. Y. See page 1012.

Massive Left Auricle. Louis Faugeres Bishop, Jr., M.D., and Andrew Babey, M.D., New York, N. Y.

ABSTRACT

The clinical features of two cases are reported and the differential diagnosis from effusions and tumors of the chest and esophagus is discussed.

DISCUSSION

Discussion of the paper, "The Results of Treatment of Cardiovascular Syphilis," by Drs. Padget and Moore.

Dr. Edwin P. Maynard, Jr., Brooklyn, N. Y.—I should like to ask Dr. Padget from what point he calculated life in those patients who had inadequate and adequate treatment. Did he take the duration of life from the time they began treatment or from the time of infection with syphilis? It is an important point in statistical analysis to date the duration of life from some definite point in the course of the disease rather than from the time the patient happens to come in contact with the doctor.

Dr. Homer F. Swift, New York, N. Y.—Was there a distinct difference in the relative comfort of these two groups of patients? Were the symptoms and signs of the well-treated patients less than those in the poorly treated group?

Dr. Julien Benjamin, Cincinnati, Ohio.—Will Dr. Padget please tell us what he considers adequate treatment; and whether he is considering as adequate treatment that received during the course of cardiovascular syphilis, or that received early in the course of the disease?

Dr. Joseph E. Hirsh, Birmingham, Ala.—Dr. Padget makes no differentiation between those patients who come in compensated and those who are decompensated on admission. My experience in the South, where we have a great number of negroes with cardiovascular syphilis, is that if the patients are compensated, antiluetic treatment may help them; if they are decompensated with dyspnea, edema, and all the classical signs of heart failure, there is no improvement. Once an individual with syphilitic heart disease becomes decompensated, he remains decompensated, despite all specific treatment, whether it be arsenic, iodides, bismuth, or mercury. We find that in such patients the mortality is practically 100 per cent, despite all treatment.

Dr. Roy W. Scott, Cleveland, Ohio.—Some ten years ago I became interested in this subject but did not follow it through, so far as therapy is concerned, as adequately as Dr. Moore has since done. We were very much impressed, and so stated at the time, that once the intervention of circulatory failure in the course of syphilitic aortic insufficiency occurred, no treatment that we were able to supply made any difference in the clinical course of the disease.

Dr. M. A. Mortensen, Battle Creek, Mich.—I should like to ask if any of these patients had antiluetic treatment prior to the discovery of cardiovascular lues. Many patients know that they have had syphilis for years and have had more or less treatment prior to the diagnosis of cardiovascular syphilis. In these cases may not the final picture be due to inadequate treatment?

Dr. Paul Padget, Baltimore, Md.—I am grateful to Dr. Maynard for bringing up the question concerning dating the duration of life. The duration of life in these patients was dated from the onset of symptoms definitely referable to the cardiovascular system, with the exception of those who, in the course of routine investigation, were found to have cardiovascular syphilis. Obviously this introduces some uncertainties, but in this series we saw no better way to meet the problem. To answer Dr. Swift, we shall later go into considerable detail concerning the ability of these patients to work. Briefly, alleviation of symptoms was a very conspicuous feature in those who were well treated and many regained ability to work. In answer to several questions about the amount of treatment—we consider adequate treatment in the presence of cardiovascular syphilis to be at least one year of continuous treatment with heavy metal and arsenicals in which the heavy metal phase in emphasized, as outlined by Moore, Danglade, and Reisinger. The minimum of the "adequate treatment" group of this series was less than that, but there were only three patients so classified who fell short of approximating what we considered to be the true minimum, i.e., a year of treatment. In regard to treatment for early syphilis, it is to be emphasized that no patient in this group had had adequate treatment for early syphilis, and only a few had had any treatment at all prior to the discovery of the cardiovascular lesions. The incidence of cardiac failure was the same in the "inadequate treatment" and "adequate treatment" groups (approximately one-fourth of each) but was higher in those who died in less than a year of observation.

Discussion of papers, "The Significance of the Electrocardiographic Changes in Diphtheria" and "The Pathological Analysis of Diphtheritic Myocarditis With Especial Reference to Electrocardiographic Findings," by Drs. Smith, Burkhardt, and Eggleston.

Dr. Arthur M. Master, New York, N. Y.—I think it is not surprising that one often fails to find pathological changes at post-mortem examination, for we know that there may be functional as well as anatomical changes in the heart muscle. In certain individuals auriculoventricular conduction defects may appear if the heart rate is speeded up by exercise or by giving amyl nitrite, but as soon as the stimulus is over, the electrocardiogram returns to normal.

Dr. Clarence E. de la Chapelle, New York, N. Y.—I should like to ask Dr. Smith whether in those hearts which had either auricular or ventricular thrombosis he found underlying changes in either the endocardium or the myocardium; also, whether in the cases that showed diffuse fibrosis, he saw any evidence of activity, either in a healing state or still fairly active.

Dr. Hugo Freund, Detroit, Mich.—I should like to ask Dr. Smith if there were any changes in the intracardiac ganglia.

Dr. W. Bernard Kinlaw, Rocky Mount, N. C.—I should like to ask if any of the patients have developed true definite block and recovered.

Dr. E. A. Burkhardt, New York, N. Y.—In the seventeen cases showing conduction changes, eleven developed an auriculoventricular block. This complication was invariably fatal. Some patients with intraventricular block did recover.

Dr. Lawrence Smith, New York, N. Y.—We have not been able to demonstrate any changes in the ganglion cells. Those studies we tried to carry out systematically, but our results have not been uniform. Apparently the lesion is one of the contractile tissue, rather than of the nerve cells proper. As far as the endocardial lesion is concerned, Dr. de la Chapelle, the changes have been minimal with one or two notable exceptions. There seems to be nothing active beyond these fibrotic sclerotic changes.

Discussion of the paper, "Peripheral Venous Phenomena in Congestive Heart Failure," by Dr. Kerr.

Dr. Jacob Polevski, Newark, N. J.—In connection with pulsation of the veins of the neck, I have seen two cases of young children with mitral stenosis in a perfect state of compensation with no evidence of pronounced right cardiac dilatation and surely no relative tricuspid insufficiency, in which the upward pulsation in the jugulars led to a diagnosis of patent foramen ovale. One of these patients subsequently died from pneumonia, and the autopsy findings confirmed the original cardiac diagnosis.

Dr. Harold E. B. Pardee, New York, N. Y.—Dr. Kerr has spoken of venous pulsations as associated particularly with right heart failure. He has also, however, mentioned the venous pulsation in association with tricuspid stenosis. I wish particularly to emphasize this latter fact because I have also noticed that there was a marked auricular venous pulsation in the veins of the neck in patients whom I have considered to have tricuspid stenosis. Two of these patients did not show any particular degree of heart failure, and in one of these the pulsation of the veins of the neck was the chief complaint for which the patient applied for treatment. This, I think, is an important diagnostic sign of tricuspid stenosis. It should be especially emphasized because in the diagnosis of this valve lesion we are in need of diagnostic signs. The similarity of the murmur to that of mitral stenosis and the frequent

presence of both lesions present a considerable problem in diagnosis. Because of the difficulty in this diagnosis I feel that I should mention another diagnostic sign which has been found in patients with tricuspid stenosis even though it is somewhat off Dr. Kerr's subject. This is the finding of a very sharply peaked auricular wave, like a high gable roof, and well over 2 mm. in height.

Dr. Simon Dack, New York, N. Y.—I should like to ask Dr. Kerr if he has been able to differentiate between functional tricuspid insufficiency and that due to organic changes in the tricuspid valve with the aid of polygraphic records. In one patient studied at Mount Sinai Hospital, on whom a post-mortem examination was made, there was a definite organic tricuspid stenosis and yet the polygraphic record was not characteristic of that condition.

Dr. William J. Kerr, San Francisco, Calif.—I would agree with Dr. Master that patent ductus arteriosus would be one of the conditions in which systolic pulsations transmitted along the venous system would be observed. With respect to functional and organic conditions of the tricuspid valve, I should like to say that we do not think, on the basis of the mechanism concerned here, that it makes a great deal of difference whether one is dealing with a relative or so-called functional tricuspid insufficiency or with one which is organic. The relative insufficiencies, of course, are usually much more transient, but in practically every patient with congestive failure based on failure of the right heart, no matter what the cause, these pulsations will be present. In patients with an organic condition of long standing, the waves may be more marked, but this is only a matter of degree. We have made use of the double wave auricular and ventricular pulsations in the diagnosis of tricuspid stenosis, and I think that that is important, as Dr. Pardee brought out.

Discussion of the paper, "The Relationship of Blood Pressure, Peripheral Vasomotor Activity, and Environmental Temperature," by Dr. Oughterson.

Dr. James P. O'Hare, Boston, Mass.—May I ask if all emotional factors were eradicated? Are there emotional factors produced in temperament, environment, etc.?

Dr. Louis F. Bishop, Jr., New York, N. Y.—Were these blood pressures recorded by any method of recording machine or were they taken with the ordinary mercurial instruments?

Dr. Ashley W. Oughterson, New Haven, Conn.—In regard to Dr. O'Hare's question, all that I can say is that as you talk to these patients, they do not mind the temperatures to which they are exposed. However, a rapid shift of 30 to 35° F. involves some little discomfort. If, for example, patients are in a state of full vasodilatation at a room temperature of 85° to 87° F., and superimpose on that an emotional factor, you may get an immediate vasoconstriction. However, the changes initiated by emotional factors do not last over long periods. Nevertheless I should hesitate to say that an emotional factor does not play some part. As regards the blood pressure, we have no automatic device. We have tried to make many but we have not succeeded. The blood pressures are usually taken at fifteen-minute intervals; some are taken at ten-minute intervals. The temperatures are recorded continuously.

Discussion of the paper, "The Influence of the Heat Regulatory Mechanism on Raynaud's Disease," by Dr. Pearse.

Dr. Irving S. Wright, New York, N. Y.—I was very much interested in this paper. There is one problem which I should like to bring to Dr. Pearse's attention. During the past several years, we have seen an occasional patient suffering from atypical Raynaud's syndrome in whom it has been impossible for us to induce

spasm purely by the maintaining of the hands in very cold water of sufficiently low temperature to induce spasm of the vessels in the usual patient with Raynaud's disease. This aroused a considerable interest because the vessels of the extremities of these individuals could be made to go into spasm if the body was exposed to low temperature. I have been in communication with Dr. Allen at the Mayo Clinic in reference to this particular syndrome, and he reports that he has seen one or two instances of the same type. Also, I believe there is a brief note in one of Sir Thomas Lewis's articles of 1925 or 1926 in which this particular syndrome, which varies somewhat from the usual Raynaud's syndrome, is mentioned.

Dr. S. Minowitz, Brooklyn, N. Y.—A doctor in Vienna called attention some years ago to a paradoxical reaction occasionally occurring in Raynaud's disease. I wonder if the essayist has observed such a thing.

Dr. William J. Kerr, San Francisco, Calif.—This is an interesting paper that Dr. Pearse has given us this morning. With respect to the emotional side in this disease, I should like to say that in a series of cases which Sir Thomas Lewis and I studied in 1928-1929, there was one patient in whom the emotional factor was very strong, and there was no doubt that with the patient in the proper environmental condition in a warm room, one could bring on the attacks by emotional disturbance. Quite recently I saw another woman with Raynaud's disease who was quite emotional and who had, we discovered on further study, a very definite anxiety neurosis. This patient came into the clinic one day in an attack of cyanosis and all the characteristic signs, and we observed at the moment that she had symptoms of tetany. Being somewhat interested in this condition we had this woman hold her breath for about 35 seconds, at the end of which time the attack went off completely. The hands and fingers became a bright pink color and seemed to be quite warm, and then she complained of throbbing and burning. In a study of these patients with anxiety states, one very often finds that they have hyperventilation and that they blow off excessive amounts of carbon dioxide which results in a relative alkalosis. Among the patients in our series, about 80 or 85 per cent will be found to have no free hydrochloric acid in the stomach and to show an alkaline urinary reaction. I would like to suggest to Dr. Pearse that if he would study some of the patients that he mentioned and find out about their gastric acidity he might get some interesting clues, but he may find those patients who did not respond after meals, as he anticipated they might, would not have free hydrochloric acid, and, if he gave them free hydrochloric acid, they might have a very remarkable response.

Dr. Ashley W. Oughterson, New Haven, Conn.—I should like to ask Dr. Pearse if he has studied weight gain and weight loss. We have one patient in whom we were able to obtain cooperation and who gained 20 pounds in about two months. That was under all sorts of therapy, as she received thyroid and insulin to stimulate her appetite, and we also increased her clothing. Her general vasomotor response, however, was very good. Another phase is that our psychiatry department has been interested in the emotional disturbances in relation to blood and fats. Some of us on a low caloric diet lost 15 pounds one month and gained it back the next. We took temperature records during the time and found there was a striking correlation between peripheral vasomotor activity and weight loss. There was also a very striking drop in blood fat during the time, and an increased irritability. Whether that would remain over a long period of weight loss or not, after one had become adjusted to the new level, I do not know.

Dr. George E. Brown, Rochester, Minn.—I want to congratulate the essayists on the excellence of their work. Those who have not followed these lines of investigation will appreciate the new thoughts and the new principles that are developing from these studies.

It is worth a moment's time to restate the problem. We have accepted, since the time of Raynaud, that Raynaud's disease is a vasomotor disorder attributable to some hypersensitivity or overactivity of the sympathetic mechanism. Sir Thomas Lewis threw a sceptical note into the assembled opinion concerning this respected tradition. He found that some patients with Raynaud's disease reacted to local stimuli following interruption of the sympathetic pathways. He postulated some fault of the peripheral vessels as the primary factor in this disease. This observation immediately started us thinking. As a result, many new, interesting facts are developing.

Now it is unquestionably true that if lumbar sympathetic ganglionectomy is performed in cases of Raynaud's disease, vasoconstrictor color reactions are never effected by cold or lowered environmental temperature. Following removal of cervical and upper thoracic ganglia, with complete removal of the vasomotor fibers to the hands, there is a certain number of cases in which cold produces ischemic color reactions. There is also a group of cases in which these reactions are abolished. It is the former group that requires further explanation. The work of Dr. White and Dr. Freeman may furnish the answer. They have shown that the sympathectomized vessel becomes hypersensitive to epinephrine and that color and temperature responses remaining after operation can be produced by stimuli causing an outflow of epinephrine. Why the upper and lower extremities behave differently remains an enigma.

As I said before, this problem may not be of broad, clinical interest at the moment. Future work along these lines may be applicable to the questions of hypertension and of many clinical phenomena that involve reactivity of the blood vessels.

Dr. Herman E. Pearse, Rochester, N. Y.—To take the questions in chronological order, that of Dr. Wright concerning cases in which there is no response to cold is first. In this reaction let me warn of the phenomenon of overcooling of which Dr. Kerr is so well aware. If the extremities are cooled below about 13° C., there is then the reaction of dilatation rather than constriction. So, in testing with cold, one has to be careful not to overcool the extremity below this critical temperature. However, it is observed that an occasional patient will not respond to an appropriate degree of cold under test conditions. I have observed the paradoxical reaction to heat but have not studied any such patients. I am very much interested in Dr. Oughterson's comment about the gain in weight, because there is a linkage between the psychic personality and the general bodily state of these individuals who have exaggerated phenomena, just as there is a linkage with body type in gallbladder disease, in duodenal ulcer, in Graves' disease, and so on. And it is true that one means of amelioration of symptoms is to have the patients gain weight. I have found it rather difficult to accomplish this because they are kinetic individuals and do not gain weight easily. Finally, I am very much indebted to Dr. Kerr for his suggestion of the achlorhydria, and he may be assured that I will investigate it. One must consider many factors in these individuals since it is my feeling that, though we use the term "Raynaud's disease," perhaps it is not a disease entity but a symptom-complex in which there are diverse motivating factors.

Discussion of the paper, "Observations Upon Electrocardiographic Tracings Obtained by the Use of Esophageal Leads in the Human Subject," by Dr. Brown.

Dr. Arthur M. Master, New York, N. Y.—Very many interesting facts have been brought out. On the other hand, there is a little difficulty in using the esophageal lead. I wonder if Dr. Brown has made comparisons with graphs obtained by chest leads, particularly when one electrode is placed on the back at the level of the third, fourth, or fifth dorsal vertebra. Chest leads are very easy to use whereas the esophageal lead may be difficult.

Dr. Meyer Sclar, Brooklyn, N. Y.—I wonder whether Dr. Brown noticed any marked increase in the extrasystoles as the result of the contact of the esophageal electrode to the heart. Is it not possible that some of the changes he observed are due to the nervousness, the tension which the patient is under, while having this foreign body in his esophagus?

Dr. Samuel S. Levine, Boston, Mass.—Did Dr. Brown have an opportunity of taking simultaneous leads in the flutter case so that he could tell when the flutter wave begins? When flutter was first described by Jolly and Ritchie, a controversy developed shortly afterward, whether the P-wave begins at the top, finishes on the top, or whether it begins at the bottom and comes up and goes down again. Being somewhat contrary-minded, in a publication about twenty years ago, I thought it was neither one nor the other and that it began halfway down on the down stroke of the flutter wave. The reason for that is that in almost all flutter curves, you see a hesitation on the down stroke. Now Dr. Brown has, I think, an opportunity here to settle this point as to where the flutter wave begins.

Dr. A. E. Turman, Richmond, Va.—I should like to ask Dr. Brown the dosage of quinidine used in his treatment.

Dr. W. Hurst Brown, Baltimore, Md.—The question was asked whether there is any similarity between the auricular curves in chest and esophageal leads. There is no resemblance between such curves. The P-waves in the chest leads, while frequently biphasic, are of small amplitude and ill defined in form.

The esophageal electrode may, I suppose, be considered in the rôle of a foreign body in the esophagus. The point has been raised as to whether it may give rise to extrasystoles in the heart. I have observed no instance where extrasystoles occurred in the esophageal lead when they were not already occurring in conventional leads. I would emphasize that the electrode is small and smooth and that in situ it occasions very little discomfort. The passage of the electrode may be compared in technic with the introduction of duodenal or stomach sampling tubes: in my experience it is in fact easier to pass the esophageal electrode.

I regret that I have not yet obtained the material necessary to enable me to answer Dr. Levine's question. The intrinsic wave in flutter is, of course, directed upward. A comparison in the time relationships of these intrinsic waves to the flutter waves of conventional Lead II can best be made by the study of simultaneous tracings on the two-stringed galvanometer, and this I have not yet done.

The patient with flutter, who was treated by quinidine therapy and on recovery showed occasional absence of the P-wave, received in all 14.7 gm. of quinidine sulphate in a period of eight days.

Discussion of the paper, "The Protective Effect of a Collateral Vascular Bed Upon Coronary Occlusion," by Dr. Beck.

Dr. Harold N. Feil, Cleveland, Ohio.—Mr. Chairman, I would like to say a few words about the patients on whom Dr. Beck has tried this operative procedure. The first was a man aged forty-eight years, a farm laborer, who had had typical substernal pain on effort of two years' duration. This man finally had to give up his job, and entered the hospital. His blood pressure was within normal limits. There was no evidence of circulatory failure, and no other cause for the substernal pain could be made out after complete study. There was no evidence of failure, and his circulation time was within normal limits. After the exercise tolerance test, he had substernal pain, fatigue, exhaustion, and great dyspnea. He was operated on, and now, four months after the operation, we put him through the step test and find that he has a distinctly improved tolerance for exercise; he is up and

around the ward helping as a ward orderly. The pain and discomfort which he had in the chest are gone completely, even on moderate exertion. We have not tried him out on any extreme exertion, but work as a ward orderly caused no distress. From the clinical point of view, I should say that the results were highly satisfactory at the end of four months. Certainly, subjectively he is tremendously improved, and objectively the operation did no harm.

A second patient, a fifty-three-year-old man, came from a family with a history of coronary disease. Two brothers had died and a sister had met sudden death. This man, a salesman, finally had to give up his work over a period of three years because of pain on the slightest exertion. Like the first patient, he had no evidence of failure. The circulation time was within normal limits, the metabolism was normal, and there was no evidence of disease of the gastrointestinal tract that could in any way explain the symptomatology. He withstood the operation very well. At the end of five days, he suddenly developed evidence of occlusion of the aorta at its bifurcation and died within twelve hours. At post-mortem examination, it was found that he had excellent adhesions as the result of the operative procedure, and he had a large thrombus at the bifurcation of the abdominal aorta over an atheromatous area. We cannot say very much about the results in this second case, except, first, he withstood the operation very well, and apparently was recovering; and, second, the adhesions produced operatively were well on their way to formation.

The third patient was a fifty-one-year-old executive with a typical history of angina of effort of seven years' duration. Usual medical therapy gave only palliative relief. Finally, two years ago, he was forced to give up all activities. One year ago he had a total thyroidectomy. This procedure was followed by relief from pain, but, when an effort was made to relieve him of his myxedema, pain reappeared. After one year's futile effort to establish a favorable dose of thyroid he was operated on by Dr. Beck. He withstood the operation very well and has made an uneventful recovery. Now, six weeks later, he has had no recurrence of pain, although the dose of thyroid which produced pain preoperatively is being administered. Also activities about the hospital, which brought on pain before operation, are tolerated.

A fourth patient, a surgeon aged fifty years, with definite subjective and objective evidence of angina, was operated on. This man, suffering for five years, refractory to medical therapy, finally became totally disabled about three and a half years ago. He gave a history suggesting coronary thrombosis two and one-half years ago. There was no evidence of congestive failure, and the circulation time was within normal limits. His convalescence from the operation was uneventful, and now, five weeks later, he is comfortable and has but rare mild anginal attacks.

In summary, four patients with severe coronary sclerosis with incapacitating angina have been operated on with operative recovery in all cases. One patient died five days later from an aortic thrombosis at the bifurcation of the abdominal aorta. The other patients at this early date have all shown striking improvement, and it is hoped that the new coronary circulation will be of lasting aid to the heart.

Dr. E. Cowles Andrus, Baltimore, Md.—It seems to me Dr. Beck is to be congratulated upon the careful, philosophical fashion in which he approached the problem. The possibility of developing a collateral circulatory bed in the heart is, of course, of fundamental importance. There are one or two questions I would like to ask. It is too much, of course, to demand that the exact conditions which the need for such an operation would imply be reproduced in experiments. But in coronary occlusion or in gradual diminution of the coronary flow in individuals with coronary sclerosis over a period of years, there is a time element which is difficult to meet, I suppose, in the acute experiment. Specifically, I personally should like to know the lapse of time between the implantation of this graft or the procedure itself

calculated to develop a collateral circulation and the ligation of these arteries. Is it possible to get the graft to take *ex post facto,* so to speak?

The problem represented by acute coronary occlusion leaves the heart with an infarction upon which collateral circulation must be developed. The problem, as I understand it, as presented by Dr. Beck, is, first, the development of collateral circulation and later the superimposition of a reduced coronary blood supply.

I should like to mention a few experiments by no means so complete as those of Dr. Beck's, which Dr. Rienhoff has been undertaking in Baltimore and with which I have been associated—the implantation of the omentum through the central tendon of the diaphragm about the heart. We can only say that judged by the effect of ligating the major arteries, a collateral circulation has developed. We have no injection preparations as yet. In stripping the graft from the heart, it appears that the blood supply has passed from the graft into the myocardial tissue.

Dr. George Fahr, Minneapolis, Minn.—In evaluating this or any other procedure for the establishment of a collateral circulation in the heart, it is necessary to know how long it takes to establish this adequate collateral circulation. I am therefore asking Dr. Beck to inform us how long it takes to establish this collateral circulation from the outside. I am asking this because G. von Anrep, who has done a number of these experiments on dogs, assures me that it takes over a year to establish an adequate circulation.

Dr. Louis Gross, New York, N. Y.—It would be of interest to learn whether Dr. Beck has attempted to ascertain the changes which may take place in the blood vessels of the dog's pericardium following gradual occlusion of the coronary vessels without previous epicardiectomy. In the human being, I have been able to show that if coronary sclerosis and occlusion take place slowly, there occurs quite a considerable development of epicardial vessels. I have also shown that intramyocardial anastomoses become increasingly prominent with advancing age. Apparently this is a normal physiological process and takes place slowly. With this in mind, Dr. Lester Blum and I became interested in the question of experimentally increasing these intramyocardial collateral vessels at a rate considerably faster than that which apparently occurs in the human heart. For reasons which I have not time to go into, we finally decided that a reasonable approach would be to tie off the coronary sinus in dogs. This was performed in a large number of dogs with extremely interesting results. Almost immediately following the coronary sinus tie-off, the coronary artery tree becomes enormously increased in extent. This can be determined easily by injection studies.

We then subjected these dogs to the crucial experiment of sudden occlusion of the most important coronary branch—the left anterior descending. In these experiments we were careful to tie off the vessel and cut it between ligatures. As is well known, such ligation of the left anterior descending coronary branch performed in the intact animal produces a large infarct almost invariably. However, when we performed this operation on a number of dogs which had been previously subjected to coronary sinus tie-off, either the infarct was completely missing, or, in fewer instances, the infarct which resulted was considerably smaller than is generally found in unprepared animals. In other words, coronary sinus tie-off in the dog's heart so completely transforms the coronary artery tree that it is either impossible or very difficult to produce an infarct in the heart so treated even by employing one of the most severe and dramatic methods at our disposal (sudden occlusion of the left anterior descending coronary branch).

It seems, therefore, that by some such means, at least in the dog's heart, one is able so to affect the myocardial vessels as to stimulate the development of a compensatory vascular tree which apparently can function under extremely adverse

circumstances. It is of interest that in the dog the operation takes a maximum of twenty minutes to perform, requires no splitting of the ribs, and leaves the pericardium relatively intact.

Dr. C. W. Greene, Columbia, Mo.—I have watched the development of the announced results of Dr. Beck with great interest. It seems to me a plausible and hopeful method of producing some slight improvement in a damaged coronary circulation. The point I raise, however, is that the data from the experiments on the injection of methylene blue seem to me to indicate rather a good collateral circulation of the anastomotic type, a relation that we have learned in recent years to be present in the dog's heart. I am slow to accept the view that the collateral circulation is stimulated by the technic of coronary obstruction used in this new operation. It is perfectly understandable why Dr. Beck should proceed from the standpoint of clinical condition of occlusion and try to imitate it; but from the standpoint of facilitating the development of an anastomosis, it does not seem necessary to occlude the coronary artery experimentally. I am wondering, therefore, Dr. Beck, if you cannot reverse the interpretation and method with greater hope of quickening the development of an anastomotic system by leaving the coronary circulation unobstructed.

Dr. Claude S. Beck, Cleveland, Ohio.—In answer to Dr. Andrus' question, I might say that when a portion of the myocardium is destroyed by infarction the damage is irreparable. The scar produced by an infarct does not possess the property of contractility. The blood supply to such scars is not nearly so essential as is the blood supply to functioning muscle. The operation that I am developing will give the best results in those cases in which fibrosis of the myocardium is not far advanced. Obviously, little can be expected from the heart when myocardium has been replaced by scar and fat. I believe the operation can prevent further replacement changes in myocardium.

The experiments that were illustrated by colored lantern slides were carried out in this rotation: The epicardium was stripped off the heart at the first operation and adjacent tissues were sutured to the myocardium. For the collateral bed we used fibrous pericardium, pericardial fat, pedicle grafts of skeletal muscle from the chest wall and omentum brought up through an opening in the diaphragm. Usually at the same operation we placed silver bands around the right coronary artery, the descending ramus of the left, and the circumflex ramus of the left coronary artery, and these silver bands were slightly compressed so that partial occlusion was produced. The second operation was carried out after an interval of several months. At the second operation one of these major arteries was completely occluded. We found by experience that we could occlude the descending ramus of the left or the circumflex ramus of the left coronary artery or the right coronary artery as a routine without fatality if the occlusion was carried out in two stages. Further occlusion was done in subsequent operations.

The earliest evidence of anastomosis between extracardiac and cardiac vascular beds was after two to three weeks. In one experiment we could demonstrate dye in the myocardium two weeks after the collateral vascular bed was produced. The dye was injected through the extracardiac vascular bed. In another experiment anastomoses were observed three weeks after operation. The anastomoses grow larger as time elapses. I hesitate to make the direct application of these observations in animals to the human patients upon whom I carried out my operation. Our three patients stated that they felt the beneficial effect of the operation as early as three or four weeks after the collateral bed was attached to the heart.

The evidence presented by Dr. Gross is extremely interesting to me. Perhaps in the future it may have some clinical application. At the recent meeting of the

American Surgical Association I presented some of our work, and the question was asked me by several surgeons what happens if you ligate the vein along with the artery. During the war Sir George Makins advocated ligation of the corresponding vein when an artery had to be ligated. He has shown that the incidence of ischemic necrosis in an extremity is reduced by ligation of the vein. Dr. Gross has shown that this principle can be applied also to the heart. Venous ligation increases the peripheral resistance and would tend to keep the blood in the capillary bed of the heart. It may be of value in distributing the blood to various parts of the myocardium, but I do not see how occlusion of the vein can bring additional blood through the stenosed coronary arteries to the heart. Our experiments have pointed out the importance of distribution of blood to various parts of the myocardium. A relatively small area of myocardium made ischemic will bring the heart to a standstill. The experiments illustrate the significance of localized ischemia in contrast to generalized ischemia of the myocardium. I believe Dr. Gross' results can be explained on the basis of an improved distribution of blood to various parts of the myocardium rather than on the basis of an augmented arterial flow.

I do not know whether I got Dr. Greene's question. It is a fact well established by surgeons that partial occlusion of an artery is followed by the development of a compensatory circulation.

I would like to make these concluding remarks: I believe we have produced a new blood supply to the heart by operation. I do not believe our experience is sufficient to say that we have corroborated the experimental facts on patients suffering from sclerosis of the coronary arteries. Until this has been accomplished, the operation should be regarded as an experimental procedure. The operation is not without hazard and I hope surgeons will not accept the procedure until it has been satisfactorily applied.

Addendum: During the interval of several months since this presentation was made I operated upon several patients with coronary sclerosis. The beneficial results of the operation are exceeding my expectations. The degree of improvement following operation is most gratifying. It seems to me now that a new field of surgery has been opened up.

Discussion of the paper, "A Follow-Up Study of Sixty-Four Patients With Right Bundle-Branch Conduction Defect," by Drs. Wood, Jeffers and Wolferth.

Dr. Arthur M. Master, New York, N. Y.—I had occasion this morning to mention some cases of normal people who, when the rate was increased by drugs or exercise, developed intraventricular block, and, as the rate slowed down, the electrocardiogram became normal. Perhaps they fall into this class. Physicians who have been interested in electrocardiography have known that there was a type of intraventricular block as described in which the prognosis was good. I think there have been a few publications to this effect but in no case in detail or in a follow-up study. I think that Drs. Oppenheimer and Mann reported this before the Society of Experimental Biology and Medicine, and they called this the S-wave type of intraventricular block because the notching and the slurring and the widening are in the second half of the QRS group. It seems to me that in just this point emphasis must be made. An electrocardiogram that shows the ordinary type of bundle-branch block is, I think, of great significance, but if the widening and notching and slurring are in the second half of the QRS complex the patient's prognosis is much better.

Dr. Samuel S. Levine, Boston, Mass.—This paper, I think, calls attention to the fact that there is room for ordinary medical sense in sizing up cardiac problems. The electrocardiograph tests certain things. When it does not altogether fit in with what you perceive by other judgment, it is worth while to look with sus-

picion on the interpretation of the cardiogram. A contribution like this adds emphasis to just what we mean by clinical sense. We are attaching too much importance in a prognostic sense to the cardiogram. Diagnostically, we have been helped a great deal. It is very curious that the prognosis in patients with angina pectoris, which I reviewed a few years ago, was better in those patients with definite angina pectoris and abnormal electrocardiograms than it was in those with normal electrocardiograms. A follow-up study of 100 patients with angina pectoris revealed that those who had wide QRS complexes or bundle-branch block lived longer than those patients with angina pectoris who had essentially normal curves. So from the prognostic point of view we are not on such very firm ground. Diagnostically, I am aware that electrocardiography has been helpful. Ordinary clinical sense is still an important factor in judging prognosis, and it is difficult enough at the best.

Dr. Meyer Sclar, Brooklyn, N. Y.—I had a patient come to me in 1933. He brought with him an electrocardiogram taken in 1922, which showed a marked right bundle-branch block. When I saw him in 1933, I was surprised; I was under the impression he should have been dead by that time. All he complained of was some vague precordial discomfort, and he was able to carry on his usual routine as an insurance man. I immediately communicated with a number of the leading cardiologists in the country and received several replies, among others from Dr. B. S. Oppenheimer, of New York, and Dr. Paul D. White, of Boston, and each informed me that he had had quite a number of patients of right bundle-branch block, and that they had all carried on fairly comfortably, actively, and usefully. I am glad that Dr. Wood and Dr. Wolferth throw a good deal of optimism upon the right bundle-branch block.

Dr. Wallace M. Yater, Washington, D. C.—These observations fit in very well with the fact that on careful sectioning of the conduction system of the heart one may find in a surprising number of cases extensive and very severe lesions of the bundle branches without apparent involvement of the myocardium, and it is quite possible that these changes have existed for years. It would seem that the conduction system is the first part of the heart to feel a diminution in blood supply. It is interesting to note also that these patients may show various types of conduction disturbances without myocardial insufficiency. As I said last year at the American Heart Association meeting, we are making too many electrocardiographic diagnoses without a basis in anatomical fact. If some of us would get busier and do this type of very tedious work, I am sure we should find that these changes exist much more frequently than we have thought.

Dr. J. H. Crawford, Brooklyn, N. Y.—About four years ago I saw a young woman who had been rejected as a school-teacher on account of a slight murmur in the region of the third and fourth left interspaces close to the sternum. She had an electrocardiogram exactly the same as Dr. Wood has described. She had been a champion in many different types of athletics which must have thrown considerable strain on the heart, but she had no symptoms whatsoever. There was no cardiac enlargement and nothing to indicate that there was anything wrong with the cardiovascular system. Since then her activities have been unrestricted, and she has had absolutely no symptoms. It is the same type of case as those which Dr. Wood has just described.

Dr. Harold E. B. Pardee, New York, N. Y.—Dr. Wood has certainly impressed us with the idea that this type of bundle-branch block is associated with a better prognosis than the other type. I do not think, however, that he wished to impress us with the idea that it must have a good prognosis, nor do I think he wished to impress us with the idea that the other type must have a bad prognosis. I am

quite sure than everyone who sees many electrocardiograms will find that he has seen a number of curves of the other type in persons who are just as free from symptoms of cardiac failure as those which have attracted attention here. I would like to know what Dr. Wood's experience has been in this regard. I feel also that, when one talks about prognosis in electrocardiographic features, it is very much like talking about prognosis in mitral stenosis or more like talking about the prognosis of a certain type of heart murmur. It does not seem to me to be a logical thing to do. There has been a great deal of that sort of talk, and I feel that it is all wrong. Prognosis must depend upon the patient who has heart disease, not upon any isolated finding which he may have. If there is only one finding, it is well to put that into the picture, but that is not the whole picture; the patient is the whole picture.

Dr. John Wyckoff, New York, N. Y.—In the Cardiac Clinic in which I have worked, we have had a rule that no diagnosis or prognosis must ever be made on a single symptom or a single physical sign. It seems to me that this paper and Dr. Levine's and Dr. Pardee's discussion of it show that that rule is a fairly safe one to follow.

Dr. Francis Clark Wood, Philadelphia, Pa.—The question was raised as to whether any of these patients had temporary bundle-branch block and therefore were in better condition than if they had had permanent block. Three of the sixty-four patients showed temporary returns to normal intraventricular conduction from time to time. The rest probably had permanent conduction defects since none of their tracings showed normal QRS complexes.

Discussion of the paper, "The Effect of Irregular Cardiac Rhythms on the Minute Volume Output of Blood from the Heart in Human Beings," by Drs. Stewart, Crane, Dietrich, and Thompson, New York, N. Y.

Dr. Samuel S. Levine, Boston, Mass.—I am not clear whether Dr. Stewart wants us to believe that it is well for the heart to work hard. The question is: Is it better for that heart to be doing more work? If at the end of the experiment the heart has been restored to a normal rhythm and the amount of foot pounds or work the heart has done has increased, it sounds as if it is a good thing, but it is not necessarily so. The opposite of that is what we are trying to do in resting the heart. If improvement takes place from thyroidectomy, it takes place because the work of the heart is diminished, not because it is increased.

I am putting this in the form of a philosophical question. It would certainly seem as if fibrillators are better off in many instances when the heart is regular, but I do not know that the theoretical evidence that the heart is doing more work is adequate proof that it is better for that heart. I can readily conceive of the fact that the heart is better off eventually, over years, if it is doing less rather than more work.

Dr. Harold J. Stewart, New York, N. Y.—For a given size of the heart at rest, a certain amount of work should be performed. That falls in line, of course, with Starling's law of the heart. Now it has been found, according to Starr and his associates' work, that when the size of the heart is so large that the work which that large heart performs is not commensurate with the size of that heart, those patients either suffer from heart failure or are threatened with heart failure.

Discussion of the paper, "The Clinical Value of the Fourth Lead, as Observed in 3000 Ambulatory Patients," by Drs. Lundy, McLellan, Bacon, and Merchant.

Dr. Arthur M. Master, New York, N. Y.—I recently reported fourth leads in normal individuals. I think that more harm than good was done because I would

report that in normal persons the Q-wave, for example, in the fourth lead is at least two millimeters in size. Hence many think that, if a Q-wave is of one millimeter in size, the patient has an abnormal heart. I think it brings up the point that Dr. Levine and Dr. Pardee brought out, but perhaps a little differently. I think the electrocardiogram and the electrocardiograph are all right, but I think the difficulty lies in interpretation. You have to know the normal electrocardiogram, and you must use a knowledge of clinical medicine in the interpretation. Here are some more interesting things that we learned about the fourth lead. We found, first of all, that you do not need the fourth lead except in few cases. If you have an entirely normal three-lead electrocardiogram but feel clinically there is heart disease, then take a fourth lead. We found the only thing that could be depended upon in the fourth lead was the upright T-wave. If the T-wave is upright, we feel that is abnormal. On the other hand, here again if you take electrocardiograms in children with an electrode anywhere between the sternum and the apex or beyond, you find upright T-waves in more than 60 per cent of the cases. There have been publications on the value of a fourth lead in rheumatic heart disease, and the diagnosis has been made on a T-wave that is upright in the fourth lead, whereas we know that in young children this upright T-wave is a normal finding. I should like to describe the way I feel about the fourth lead by bringing up the case of a patient with a dropped heart. Now a patient with a long narrow heart often has a right ventricular preponderance on the electrocardiogram; he often has a large auricular wave and often has a blowing systolic murmur at the apex, and yet we know he has not any heart disease. Those three phenomena are associated with his dropped heart. In a similar manner you must use your clinical judgment when drawing conclusions from the electrocardiogram.

Dr. Simon Frucht, Brooklyn, N. Y.—Soon after Wolferth and Wood published their article on Lead IV with reference to coronary thrombosis, I began a study of Lead IV in other conditions. I found that a deepened Q_4 was present in practically very case of mitral stenosis. In hypertensive heart disease Q_4 was absent.

The reader of the paper presented an electrocardiogram of a young child which showed a right axis deviation and a deep Q_4. As the child grows older, the position of the heart changes, and the electrocardiogram assumes a more normal form. The form of QRS in Lead IV varies according to the position of the heart and the state of the myocardium. Rotation of the heart to the right or left causes Q_4 to increase or decrease in amplitude. Pronounced mitral stenosis, in which the heart enlarges to the right and rotates to the left, shifting the apex backward, gives rise to a deepened Q_4 together with a right axis deviation. Long-standing hypertensive heart disease, in which the heart enlarges to the left and rotates to the right, bringing the apex forward, gives rise to an absent Q_4 in conjunction with a left axis deviation. Lead IV visualizes anterior and posterior axis deviations.

Dr. Charles C. Wolferth, Philadelphia, Pa.—It is many years since Einthoven and his successors began to work on the standardization of limb leads of the electrocardiogram; nevertheless, it has been shown today that their work has not been completed.

In the attempt to standardize the so-called fourth lead, we are faced with a complexity that does not obtain in the study of the three limb leads, namely, the position of application of electrodes. This subject has been referred to this afternoon. Everyone who has looked at hearts under the fluoroscope knows that from patient to patient the position of the apex varies tremendously. We have concerned ourselves with this problem of standardization of chest leads for four years. My colleagues, Drs. Wood and Edeiken, have come to the conclusion that it is important to determine the position of the apex by fluoroscopy so that its relation to the

position of the anterior electrode is known. This precaution is not often necessary in clinical work since the position of the apex can usually be located with reasonable accuracy by palpation.

If the admittedly rough standards now available are adhered to, chest leads have diagnostic value in addition to their usefulness for the demonstration of acute or old myocardial infarction. Thus, in a certain proportion of patients with angina pectoris, one gets T-wave changes such as are not encountered in normal controls, provided that the electrode is accurately applied over the apex. Upright T-waves in Lead IV, under these circumstances, have significance comparable to that of inverted T-waves in Leads I and II. Furthermore, when the electrodes are accurately applied, the absence of an initial downward deflection also has considerable significance. However, neither of these abnormalities as an isolated finding warrants the diagnosis of myocardial infarction. It is of interest, however, that the combination furnishes an almost certain indication of anterior infarction.

Dr. Clayton J. Lundy, Chicago, Ill.—I can add that this paper attempted to show the electrocardiographic findings in clinically diagnosed cases. We did not make the diagnoses upon the basis of the electrocardiographic findings.

Discussion of the paper, "A Study of 150 Cases of Coronary Thrombosis Treated With Low Calorie Diets," by Drs. Master, Jaffe, and Dack, New York, N. Y.

Dr. Jacob Polevski, Newark, N. J.—Mr. Chairman, about a year ago at the annual meeting of the American Therapeutic Society,* I reported a diet that I instituted at our hospital several years ago. I called attention to the fact that by reducing the weight of the patient we are very often able to approach an equilibrium between the heart's ability to supply and the tissue's demand.

This diet consists of a five-day subsistence on fruit and vegetables with the exclusion of other foods and fluids, following which period food is added sparingly and gradually. The loss of weight during the first five days frequently amounts to between six and ten pounds. The amount of fluids added subsequently is never to exceed two, or at the most four, glasses daily. A ten- to twenty-pound reduction is not uncommon within a period of two to three weeks. With this diet we seldom had to resort to mercurial diuretics for the relief of the edema and with the loss of actual body weight and tissue fluids, a marked drop in both systolic and diastolic pressures was very often observed; this was often accompanied by marked improvement in the general condition of the patient. These patients are advised subsequently to have one or two exclusive fruit and vegetable days every week.

Dr. Louis A. Kapp, New York, N. Y.—I should like to ask Dr. Master whether blood sugar determinations were made in the series, and, if so, were there any hypoglycemic conditions observed during the treatment by a low calorie diet. From the investigations by Proger and others we know that some patients if put on a restricted calorie intake react with a lowering of their basal metabolic rates, others do not. The change in the basal metabolic rate in its turn frequently affects the blood sugar levels, blood cholesterol, etc. It, therefore, seems to be of clinical importance to find out whether any significant variations in the blood chemistry data in the individual patients were present in the course of the outlined treatment. While it is generally conceded that a low calorie diet is beneficial to cardiac patients, one would hesitate to go beyond certain limits. It is difficult to comprehend why 800 calorie diets were selected as a standard. I think that age, sex, weight of the patients, as well as the basal metabolic reactions and blood sugar levels, should

*Tr. Am. Therap. Soc. 34: 117, 1934.

have been considered as criteria in determining the appropriate low calorie diets in the cases. What appears to be a low calorie diet for one might be high for another patient.

One more question I would like to ask is whether any deviations from the usual successive changes in the electrocardiogram seen in myocardial infarction were noted in the patients treated with a low calorie diet. For some time I have been engaged in a study on the changes in the electrocardiogram in various blood sugar levels, especially in hypoglycemia. I wonder what experience Dr. Master has possibly had in this respect in connection with the reported method of treatment of coronary thrombosis.

Dr. Meyer Solar, Brooklyn, N. Y.—I would like to ask Dr. Master how long he keeps these patients on this diet. As soon as the patients begin feeling better, let's say the second week following the acute coronary insult, do they complain of hunger? Also, at the outset he mentioned digitalis and adrenalin are definitely contraindicated. This seems to be universally accepted. However, does he still consider digitalis contraindicated when congestive heart failure sets in, and does he still consider adrenalin contraindicated when the systolic pressure drops to 80 or lower?

While on the subject of drugs—how many cases did he find in which fibrillation began following the coronary insult, and did he use quinidine when fibrillation did set in?

Dr. Simon Fraucht, Brooklyn, N. Y.—I would like to ask how many of these patients were diabetic.

Dr. Arthur M. Master, New York, N. Y.—Naturally we did more than I could report in twelve minutes. We made blood sugar determinations, but there was no change; there was no definite drop below the normal figures. In reply to the question about the diet—of course, we were elastic. There were a few patients who were very hungry. Certainly, we gave them 1,000, 1,100 or 1,200 calories daily. On the other hand, two or three of these very hungry patients, once they experienced the benefit of the diet, refused to go back on their regular diet. We have to this day two or three patients who have remained very thin; they just won't eat. We have not followed the electrocardiograms in great detail although we have taken many. We hope to make some sort of an objective comparison with patients who have had coronary artery thrombosis and had the same regime as ours except that they have had full diets. I think we have the opportunity because Fishberg and his coworkers at the Mount Sinai Hospital recently reported some sixty cases in which they followed the same course except that their patients received the regular diet. They recorded blood pressure readings, circulation times, and other studies that we too have done. Digitalis we do think is contraindicated. We did have patients with congestive heart failure, but it wasn't necessary to give this drug. Patients stand a diuretic like mercurpurine and the acid-producing drugs like ammonium chloride much better. We are afraid, particularly early in the attack, to give digitalis. We did have five patients with transient auricular fibrillation, but they spontaneously returned to a regular sinus rhythm. We never use quinidine in any of our patients. We consider it dangerous in an acute coronary artery thrombosis. I might add, before I close, that the question is constantly put to us whether our work correlates with the work that has been done in Boston. Does this low dietary regime attain the same results that total thyroidectomy does? I do not know. I know this, however: we can over a period of several months keep the basal metabolic readings between minus 20 and minus 35. We think that the mechanism is different from the mechanism that intervenes after total thyroidectomy. In our cases there were never symptoms or signs of myxedema; the blood cholesterol was not increased; and there was no delay in the circulation time.

Department of Reviews and Abstracts

Selected Abstracts

Tennant, Robert: Factors Concerned in the Arrest of Contraction in an Ischemic Myocardial Area, Am. J. Physiol. **113:** 677, 1935.

1. Simultaneous registration of optical myograms and aortic pressure pulses indicates that abolition of myocardial contraction similar to that following coronary occlusion is produced in the presence of oxygen by potassium chloride and sodium cyanide, but not by sodium iodacetate.

2. Perfusion of a ventricular zone in the normally beating heart with sodium lactate in buffered blood-Locke's solution similarly arrests contraction. This fact, together with other experimental evidence, is strongly suggestive that excess lactate in itself is a factor in preventing contraction under anoxic conditions although it does not exclude change in pH as another possible mechanism.

Wiggers, Harold C., and Wiggers, Carl J.: The Interpretation of Monophasic Action Potentials from the Mammalian Ventricle Indicated by Changes Following Coronary Occlusion, Am. J. Physiol. **113:** 683, 1935.

Monophasic curves, recorded from a dead basal region of the right ventricle and the initially normal apex of the left ventricle, were obtained before and at various intervals following occlusion of the ramus descendens anterior.

In the analysis of such curves, emphasis is placed on two reference points viz., the moment of initial rise, A, and the point of abrupt fall toward isopotentiality on the descending limb, F. Since the interval (A-F) largely determines the area bounded by the curves, it gives more exact information of changes at the exploring electrodes than does the amplitude or contour of curves that can be recorded.

The earliest and most outstanding alteration of direct monophasic leads following coronary occlusion is the reduction in the A-F interval, with consequent decrease in the area bounded by the curve. This reduction occurs without any amplitude diminution about a minute after occlusion and is due to an earlier termination of the potential difference between electrodes. These facts indicate that monophasic potential deviations are not free from potential changes at the initial dead area, but they strongly suggest that the duration and area of the curves are significantly affected by changes under the exploring electrode.

The general deduction is made that variations in the A-F interval or duration of the curve cannot be used as evidence that monophasic curves are due solely to potential changes under an exploring electrode, unless it is shown that the rise and not only the termination changes with reference to deflections of a standard E.C.G.

A second change occurs in monophasic leads from 4 to 5 minutes after occlusion, i.e., 3 to 4 minutes after contractions have been arrested. It consists in a reduction in amplitude, without further abbreviation of the A-F interval and without change in the relation of the rise to QRS complex of an E.C.G. This obviously denotes not only a greater but an earlier development of an oppositely directed potential under the exploring electrode in the ischemic area.

The fact that monophasic curves still appreciable in size can be derived from this area until the ventricles fibrillate is a second bit of evidence that the electrode on the original area of injury exerts an important influence on the curves.

In experiments in which coronary blood flow is restored previous to fibrillation, the monophasic curves revert to their original form. This indicates that the changes described are not those due to dead tissues but to tissue the function of which has been physiologically suspended.

Wolferth, Charles C., and Margolies, Alexander: The Influence of Varying AS-VS Intervals on Split First Heart Sounds: Its Bearing on the Cause of Split Sounds and the Mechanism of the First Sound, J. Clin. Investigation **14:** 605, 1935.

1. Two cases are presented, both exhibiting complete heart-block and split first heart sounds. Heart sound tracings showed marked variations in amplitude of vibrations in each component of the split sounds. During certain ranges of P-R relations the variations in the two components appeared to be independent of each other.

2. Evidence previously obtained suggests that in cases with split first heart sounds there is asynchronism in the isometric contraction phase of the two ventricles, corresponding to the split between the two components. This affords a reasonable explanation for the variations in the two sound components, namely, that they are due to different As-Vs intervals on the two sides of the heart. Furthermore, the range of As-Vs intervals associated with increased amplitude of waves differs but little for the two components. Thus, the apparently haphazard variations in the second component are found to be of the same nature as the variations in the first component. Both components behave as do single first sounds when they are influenced by As-Vs intervals which change from beat to beat.

3. In a number of beats recorded, particularly in Case II, the P-wave falls so late with reference to the first sound component that auricular contraction could not have materially influenced this component, although marked increase of amplitude in the waves of the second component occurs.

4. In Case III (in which changes in As-Vs intervals are due to ventricular escape) independent variations in the two components of the first sound occur, which are similar to those observed in Cases I and II. This case is not as favorable for analysis as Cases I and II because the presence of ventricular arrhythmia may also influence the first heart sound.

5. Case IV shows complete heart-block and a prolonged first sound. During a certain range of P-R relations the first part of the sound is represented by vibrations with large amplitude, and during a slightly shorter range the last part of the sound is represented by sounds with large amplitude. Since this behavior corresponds to that of the two components of a split first sound during certain ranges of P-R intervals, it suggests that the prolongation of the first sound is due to slight asynchronism of the two major sound components.

6. All the findings in our cases are in accord with the postulate that one main component of the first sound is contributed by one ventricle and the other main component by the other ventricle. They lend no support to the view that both components arise in a single ventricle and, as a matter of fact, cannot be accounted for on such a basis.

7. It is suggested, on the basis of present knowledge, that major sound vibrations in each ventricle are associated with the period of rapidly rising pressure of that ventricle during the isometric contraction phase and that factors which modify the curve of rising pressure also modify production of sound. The volume of sound does not necessarily parallel the extent of rise of intraventricular pressure; the sounds are capable of varying independently of the output (as shown by optically

recorded arterial pulse waves); it is probable that the gradient of rise of pressure is the most important factor. It has thus far not been determined what structure or structures contribute the main sound vibrations in response to the application of force initiated by the contraction of the ventricular muscle upon the ventricular contents.

Resnik, Harry, Jr., and Friedman, Ben: Studies on the Mechanism of the Increased Oxygen Consumption in Patients With Cardiac Disease, J. Clin. Investigation **14:** 551, 1935.

1. The basal metabolic rate is elevated in many persons with congestive cardiac failure and declines as improvement occurs. The degree of elevation (and decline) tends to parallel the severity of congestive failure (and the extent of improvement).

2. The above observations indicate that the increased work of the respiratory muscles associated with cardiac dyspnea adds another load to an already overburdened heart. This factor of respiratory effort assumes greater importance as cardiac failure becomes worse, for the ventilation tends to rise and the vital capacity to fall, thus increasing the ratio, $\frac{\text{Ventilation}}{\text{Vital capacity}}$, in geometric proportions. Procedures which tend to reduce the ventilation (rest, morphine, venesection, paracentesis) are beneficial in part through reduction of the work of breathing.

Flaxman, Nathan: Variability of Murmurs in Mitral Stenosis, Am. J. M. Sc. 190, 396, 1935.

1. The variability of the murmurs in 237 cases of mitral stenosis is reported.

2. Auricular fibrillation was present in 46.6 per cent; it had no effect on the character or type of murmurs audible.

3. Double murmurs were found in 79 per cent.

4. Systolic murmurs alone were present in 15.2 per cent.

5. The murmurs of mitral stenosis were readily recognized by the characteristic rasping sound without resort to isolating the murmurs definitely in the cardiac cycle by timing.

Coburn, Alvin F., and Pauli, Ruth H.: Studies on the Immune Response of the Rheumatic Subject and Its Relationship to Activity of the Rheumatic Process: The Determination of Antistreptolysin Titer, J. Exper. Med. **62:** 129, 1935.

1. A method for determining the antistreptolysin titer is described in detail.

2. The natural human level of antistreptolysin determined in this way is approximately 50 units.

Coburn, A. V., and Pauli, R. H.: Studies on the Immune Response of the Rheumatic Subject and Its Relationship to Activity of the Rheumatic Process: Observations on an Epidemic of Influenza Followed by Hemolytic Streptococcus Infections in a Rheumatic Colony, J. Exper. Med. **62:** 137, 1935.

The observations presented in this paper may be summarized as follows:

A study has been made on an isolated group of children with heart disease.

All of these individuals, with one exception, were rheumatic subjects.

Many of them carried a strain of hemolytic streptococcus in the throat flora during the winter of 1934. The organism produced no detectable toxin and was not associated with respiratory disease.

Four patients contracted chickenpox during the winter months. None developed rheumatic recrudescences.

All of the individuals were in good health on March 1.

A severe epidemic of influenza began on March 22. All but six children contracted the disease. The filterable virus responsible for this outbreak was recovered.

This agent did not activate the rheumatic process. It was followed by an outbreak of streptococcus infection and appeared to facilitate its spread.

The source of these infections was not traced. They were due to a single type of hemolytic streptococcus which was a strong toxin producer. Its cultural, biochemical, and serological characteristics were different from those of the carrier strain.

Of seventeen individuals proved bacteriologically to be infected with the epidemic strain, fourteen rheumatic subjects developed acute rheumatism; two rheumatic subjects and one patient with congenital heart disease escaped.

These fourteen rheumatic attacks were accompanied by a rise in antistreptolysin titer coincident with the onset of symptoms.

In four of these attacks is was possible to exclude influenza as a causative factor.

Coburn, A. F., and Pauli, R. H.: Studies on the Immune Response of the Rheumatic Subject and Its Relationship to Activity of the Rheumatic Process: Observations on the Reactions of a Rheumatic Group to an Epidemic Infection With Hemolytic Streptococcus of a Single Type, J. Exper. Med. 62: 159, 1935.

This study of an isolated colony showed that of seven children who escaped the epidemic streptococcus infection, none developed rheumatic symptoms; and that of seventeen children who contracted the epidemic streptococcus infection, fourteen developed acute rheumatism, and three showed no recognizable rheumatic manifestations.

The seven children who failed to contract infection with *Streptococcus hemolyticus* showed clearly that susceptible individuals may live in close association with an epidemic of acute rheumatism, develop no rise in antistreptolysin titer, and maintain excellent health.

The patient with congenital heart disease demonstrated that a nonrheumatic subject may be infected with a highly effective strain of hemolytic streptococcus, develop a typical antibody response, and yet escape all rheumatic manifestations.

The two patients who, although infected with the epidemic strain, failed to show any antibody response, also failed to develop rheumatic recrudescences.

Environmental, dietary, age, and the other factors investigated did not appear to be significant in this outbreak of acute rheumatism.

Three factors appeared to determine the development of the fourteen recrudescences: (1) infection with a highly effective agent; (2) the disease pattern, peculiar to each rheumatic subject; and (3) the intensity of the immune response of the patient as indicated by the rise in antistreptolysin titer.

Kutumbiah, P.: Rheumatism in Childhood, Indian J. Pediat. 2: 215, 1935.

1. A short summary of the literature on rheumatism in India is given.

2. The contention that there is no rheumatic fever in the tropics is shown to be no longer tenable.

3. Evidence is adduced to show that rheumatic infection in childhood is common in Vizagapatam, a city situated in the tropics.

4. A brief résumé of the salient features of juvenile rheumatism as it occurs in the temperate climates is given.

5. An analysis of fifty cases of juvenile rheumatism from King George Hospital, Vizagapatam, is given.

6. The various phases of cardiac rheumatism are illustrated by typical cases from this series.

7. The age and sex incidence and incidence of polyarthritis, chorea, and nodules are discussed.

8. The frequency of cardiac rheumatism in children suffering from tonsillitis is noted.

9. Few typical radiographs and electrocardiograms of mitral disease are given.

10. It is concluded that rheumatism in childhood is very common in the Vizagapatam district, and in its essential manifestations it closely resembles juvenile rheumatism in the temperate climates.

Bland, Edward F., and Jones, T. D.: Clinical Observations on the Events Preceding the Appearance of Rheumatic Fever, J. Clin. Investigation **14:** 633, 1935.

1. There appears to be no significant clinical difference between the recurrences or recrudescences of rheumatic fever following (1) respiratory infection, (2) other forms of infection, (3) accidents or operative procedures, and (4) a single intravenous injection of typhoid-paratyphoid vaccine sufficient to cause a slight febrile reaction and chill.

2. The probable significance of these observations has been discussed. It is evident that various events precede and apparently influence the appearance of the signs and symptoms of recurrent rheumatic fever.

3. It seems desirable, in view of the observations presented, to consider the rôle of such events as nonspecific until more definite information is available concerning the etiological agent.

Seegal, David, Seegal, E. B. C., and Jost, E. L.: A Comparative Study of the Geographic Distribution of Rheumatic Fever: Scarlet Fever and Acute Glomerulonephritis in North America, Am. J. M. Sc. **190:** 383, 1935.

1. A comparative study has been made of the geographical distribution in North America of acute glomerulonephritis, rheumatic fever, and scarlet fever.

2. The case rate for scarlet fever diminishes progressively from latitude region 50 to 45 degrees to 34 to 29 degrees.

3. The yearly hospital medical admission rate for rheumatic fever in twenty-four hospitals shows a similar decrease in the same latitude regions.

4. In contrast to the diminished case frequency of scarlet fever and rheumatic fever in southern latitudes as compared with northern latitudes, the yearly hospital medical admission rate for acute glomerulonephritis does not vary significantly in the four latitude regions studied.

5. The failure of acute glomerulonephritis to diminish in frequency in southern latitudes might be interpreted as supporting the hypothesis that agents other than the hemolytic streptococcus play the chief etiological rôle in this disease. This does not seem likely, however, since considerable evidence is available incriminating the hemolytic streptococcus as the main incitant of the disease.

6. Since evidence is available ascribing etiological significance to the hemolytic streptococcus in all three diseases studied here, the variation in the geographical distribution of these diseases based upon the limited data presents a problem in specific host and bacterial interaction.

Baker, B. M., Thomas C. B., and Penich, R. M., Jr.: Experimental Carditis: Changes in the Myocardium and Pericardium of Rabbits Sensitized to Streptococci, J. Clin. Investigation **14:** 465, 1935.

1. When a heat-killed culture of beta hemolytic streptococcus is injected intrapericardially into rabbits sensitized to the same organism, an extensive carditis results.

2. The intrapericardial injection of this organism into unsensitized animals produces no such changes.

3. The changes in the hearts of the sensitized animals are characterized by an extensive, nonspecific, inflammatory reaction.

Rafsky, H. A., Bernhard, A., and Rohdenburg, G. L.: Studies in Hypertension: The Production of Experimental Hypertension and a Correlated Effect Upon the Nitrogen Distribution of the Blood Proteins, Am. J. M. Sc. **190:** 187, 1935.

1. Uranium nitrate when injected in small doses into rabbits produces nephritis with hypertension.

2. Cholesterol similarly administered produced a mild hypertension, while in a single experiment cholesterol and lecithin did not.

3. Of the amino acids injected, aspartic acid alone produces definite hypertension. At autopsy the renal lesions of glomerulonephritis were found.

4. The aspartic acid hypertension in rabbits is not dependent upon the presence of the amino or dicarboxylic group.

5. Guanidine carbonate also produces hypertension when injected into rabbits.

6. A marked fibrosis of the spleen was observed in all of the animals which developed hypertension after the injection of aspartic acid.

7. The total, the amide, the hydrolyzable, the basic amino, and the monoamino nitrogen distribution of the whole blood, of the red cells, and of the serum proteins from the same specimen of blood have been determined in seventeen normal rabbits and in six rabbits with hypertension.

8. In rabbits in which hypertension has been produced by the injection of aspartic acid, the basic amino nitrogen fraction of the serum proteins is decreased; the monoamino nitrogen fraction is increased; and there is a rise in the M/B ratio.

Meeker, D. R., Kesten, H. D., and Jobling, J. W.: Effect of Iodine on Cholesterol-Induced Atherosclerosis, Arch. Path. **20:** 337, 1935.

Potassium iodide fed in large doses for from one to three months to rabbits in which atherosclerosis had previously been induced by prolonged feeding of cholesterol does not influence the rate or nature of the involution of the vascular lesions.

Potassium iodide appears to retard the return of the cholesterol content of the blood to normal levels although it markedly depresses the ratio of the amounts of cholesterol esters and free cholesterol. It is suggested that this retardation may be due to mobilization of stored cholesterol from the tissues.

Josephi, Marion G.: Measurements of the Size of the Heart in Normal Children: A Statistical Study, Am. J. Dis. Child. **190:** 929, 1935.

A series of 418 observations on normal children is presented. These observations consist of values for height, weight, age, body surface area, and the usual measurements of the heart.

The measurements of the heart and those of the body have been correlated, and the highest degree of correlation has been shown to exist between the body surface area and the cardiac surface area.

From the relationship of the body surface area to the cardiac surface area, a quotient has been derived which has been found to be a good measure of the series.

Correlation coefficients arranged in order of their degree of relationship are:

(a) Cardiac surface area to body surface area.

(b) Cardiac surface area to weight.

(c) Cardiac surface area to height.

(d) Cardiac surface area to age.

(e) Cardiac transverse diameter to weight.
(f) Cardiac transverse diameter to body surface area.
(g) Cardiac transverse diameter to chest diameter.
(h) Cardiac transverse diameter to height.

The formula of Hodges, Adams, and Gordon for the prediction of the cardiac surface area has been applied to 100 children, and the correlation between the observed cardiac surface area and the predicted cardiac surface area has been found to be poor.

Jones, Edgar: The Demonstration of Collateral Venous Circulation in the Abdominal Wall by Means of Infra-Red Photography, Am. J. M. Sc. **190:** 478, 1935.

Ten cases are presented in which there was evidence or suspicion of hepatic disorders. Clinical findings with regard to evidences for or against associated portal obstruction, as shown by the demonstration of collateral circulation on the abdominal wall, are given. Comparison is made between the clinical findings and those obtained from ordinary and infra-red photographs of the abdomens of the patients presented. These data seem to indicate that infra-red photography may be of value in demonstrating degrees of collateral circulation which are not detected by usual clinical methods. At least it is an excellent means of recording abnormal degrees of superficial venous distention. Suggestions as to further application are made.

Abeles, Milton M., and Schneider, Daniel E.: Electrocardiographic Changes During Encephalography, Am. J. M. Sc. **190:** 673, 1935.

Twenty cases of simultaneous encephalography and electrocardiography are presented with a study of the changes in the cardiac conduction mechanism. The most common changes are those consequent upon stimulation of the pacemaker between the S-A and A-V nodes, transitory nodal rhythm. In one case ventricular extrasystole was observed, and in another auricular fibrillation. In one fatal case, death following encephalography was probably cardiac and followed the excessive injection of air with subsequent bradycardia and collapse at that period when most cases begin to show a return to normal rate. The findings are correlated with other clinical manifestations of vagus stimulation.

Norris, Robert F.: Syphilitic Aortitis in Childhood and Youth, Bull. Johns Hopkins Hosp. **57:** 206, 1935.

Two cases of syphilitic aortitis are presented. One was found in a nine-year-old girl and another in a seventeen-year-old boy. There is some evidence that the lesions were of congenital origin. These were the only cases suggestive of congenital syphilis of the aorta among 14,000 autopsies at the Johns Hopkins Hospital. That syphilitic aortitis with involvement of the coronary ostia may be, in rare cases, a cause of sudden death in young people has been emphasized. Gross myocardial necrosis and scarring in cases of syphilitic aortitis resulting from stenosis and atresia of the coronary orifices occur occasionally and should be carefully searched for.

Book Reviews

DAS ELEKTROKARDIOGRAMM. EINE VERGLEICHENDE STUDIE. By Franz M. Groedel, Dresden and Leipzig, 1934, Theodor Steinkopff.

This treatise consists of two volumes, a volume of text (358 pages) abundantly illustrated with diagrams and an atlas of 200 plates depicting the electrocardiograms discussed. The reproductions contained in the atlas were made by a special process and reach a high standard of quality.

The chief purpose of this work is to present the results of a study of what Groedel is pleased to call "partial electrocardiograms." Using oscillographs coupled to vacuum-tube amplifiers, he recorded simultaneously two standard leads, a standard lead and a chest lead, or two chest leads. Bipolar chest leads in which both electrodes were placed upon the thorax were found to yield essentially the same information as the standard leads. Unipolar chest leads in which one electrode was attached to the right arm and the other was placed upon the precordium proved to be much more useful. It is Groedel's principal thesis that when leads of this kind are employed, it is possible to record separately the right ventricular electrocardiogram and the left ventricular electrocardiogram. To obtain the former, the chest electrode is placed just to the left of the lower end of the sternum; to obtain the latter it is placed in the midaxillary line at the level of the xiphoid process. When these two curves are taken simultaneously with the camera operating at high speed, it may be seen at a glance that in normal subjects the R and T summits of the right-sided curve definitely precede the corresponding peaks of the left-sided curve. The two curves also differ greatly in general outline; in the former R and S are of approximately equal size, and there is no Q; in the latter R is very much larger than S, and a small Q is present. By dividing the height of a given deflection in the one curve by the height of the corresponding deflection in the other, various coefficients are obtained. The first part of the text deals with the form of these two "partial electrocardiograms" in normal subjects, discusses the origin of their various deflections, and presents evidence in support of the view that each of them represents the electrical activities of a single ventricle, or at least closely approaches this ideal.

The second part of the text presents a large number of clinical cases intended to illustrate the abnormalities displayed by the two "partial electrocardiograms" under various circumstances, and to demonstrate advantages over the standard three-lead electrocardiogram which they possess. This part of the book is disappointing. Three to six or more cases, regarded by the author as similar either from the clinical or from the electrocardiographic standpoint, are presented; a few brief notes regarding the history and clinical findings, a very short description of the standard and of the partial electrocardiograms, and the anatomical or functional diagnosis without comment. At the end of the presentation of each group of cases there is a brief summary which lists the different abnormalities shown by the standard and the partial electrocardiograms but usually does very little else. After covering a half dozen different groups of cases, the reader becomes bewildered and must go back and start over.

One group of cases discussed consists of six examples of "circumscribed, left-sided myocardial changes." In each of these the standard electrocardiogram displays abnormalities which have always been considered characteristic of bundle-branch

block of the common variety, but bundle-branch block is not mentioned at all. In the summary it is noted that the partial electrocardiogram of the right ventricle is widened, but not otherwise abnormal; the partial electrocardiogram of the left ventricle, on the other hand, is strikingly abnormal in several respects. That ends the matter. This is particularly puzzling when one finds that the next group discussed consists of three cases in which there was a "delay in the onset of negativity on the left side" and that it is suggested in the summary that there were localized sclerotic changes in the left ventricular muscle, possibly in the conducting system or in its neighborhood.

Approximately twenty pages of text and eighteen full-page plates are devoted to the electrocardiogram in coronary disease. The illustrations show inverted T deflections, intraventricular block, and other abnormalities, but there is not a single instance in which either the standard or the precordial electrocardiograms show changes which the reviewer would regard as characteristic of coronary thrombosis. At the end of this section it is stated that the changes in the initial ventricular deflections and in the R-T segment produced by coronary disease, right or left, are the same as those previously described as characteristic of localized myocardial changes affecting the right or the left ventricle, respectively.

With a single unimportant exception Groedel's book makes no reference whatever to the work done with precordial leads in America. In the opinion of the reviewer it advances many ideas that are sound, but comparatively few of these can be considered altogether new in 1935. It also presents many views that are certainly new, but the soundness of most of these is highly questionable. Very little evidence in the way of experimental studies, statistical material, or clinical observations supported by post-mortem examinations is offered in support of the views expressed. In this country where most electrocardiographers are using precordial leads, it is not necessary to prove that such leads are useful, and this seems to be one of Groedel's chief purposes. Nevertheless, the first part of his book is well worth reading; as to the last part, electrocardiographers with insomnia will find it not without merit.

F. N. W.

LIVING ALONG WITH HEART DISEASE. By Louis Levin, M.D., with a foreword by Thomas M. McMillan, M.D., New York, 1935, The Macmillan Co., 128 pages.

This little volume is another attempt to put before laymen, in simple language, facts concerning the heart and its disorders which may be of aid and comfort to such as have, or fear they may have, heart disease.

The task is a formidable one, beset with many pitfalls, and it is much to the author's credit that he has achieved a considerable degree of success in so difficult an undertaking.

The book displays, throughout, the reasonable, legitimate optimism which is its greatest asset. It seems safe to predict that many of its readers will be helped and few injured by its reading.

L. A. C.

DIE ELEKTROKARDIOGRAPHIE UND ANDERE GRAPHISCHE METHODEN IN DER KREISLAUFDIAGNOSTIK. By Professor Dr. Arthur Weber, Direktor des Balneologischen Universitäts-Instituts Bad Nauheim. Berlin, 1935, ed. 2, Julius Springer, 183 pages with 129 illustrations.

After reading this volume from cover to cover, one can recommend it as a valuable summary in German of the field of electrocardiography, including other graphic methods used in studying the circulatory system. In English, Lewis' *Mechanism*

and Graphic Registration of the Heart Beat is a much more complete and stimulating book, and contains almost everything of value in this field up to 1925. In the German language, Wenckebach and Winterberg's *Die Unregelmässige Herztätigkeit* is also a far more valuable and original work, but appeared as long ago as 1927. Compared with these two books Weber's monograph is briefer than either, has brought the subject up to date (and considerable new work has appeared since 1925 and 1927, respectively), and above all has stressed the physical foundation upon which these instrumental methods of cardiac diagnosis rest. The peculiar value of the book is the detailed description it gives of various types of apparatus and the aid to those practitioners who have no fundamental knowledge whatever of the principles involved in their construction and use. Whether it will ultimately be important for the practitioner to read the details of such instruments as the cathode ray oscillograph, Duchosal's ingenious ink-writing electrocardiograph, and the many types of amplifying electrocardiographs which are described is open to question, but it can do him no harm. The text is profusely illustrated with graphic records; especially noteworthy are the heart sound records; but the technic of these cannot compare with that quite generally seen in this country. The references in Weber's book to scientific and original work by English-speaking authors suffer when compared to those in German. Thus, of 347 references in the bibliography only 36 are to American or British authors. Certainly no one who has lived through the history of this subject would maintain that these figures fairly represent the relative value of the contributions of the two groups. On the whole, however, the monograph presents a straightforward, sound, useful summary of the subject which will naturally be of most value to German readers.

B. S. O.

La Cianosis De Los Cardiacos Negros de Ayerza: Su Estudio Semiologico, Clinico y Fisiopatologico. By Eduardo L. Capdehourat, Jefe de Clinica de la Facultad de Medicina, Buenos Aires, 1934, Aniceto Lopez, 374 pages with 48 illustrations, paper bound.

This study of the "black cardiacs" of Ayerza is a distinct contribution to the knowledge of the pathological physiology and pathogenesis of this obscure and interesting syndrome.

L. A. C.

Klinik und Therapie der Herzkrankheiten. Vorträge für Praktische Ärzte. By Privatdozent Dr. D. Scherf, Assistent der I Medizinischen Universitäts-Klinik in Wien. Vienna, 1935, Julius Springer, 210 pages with 10 illustrations.

Doctor Scherf has provided a manual on the diagnosis and management of heart diseases which is much more important than the unpretentious form of the book would imply. It contains the material of the series of lectures offered by him annually as part of the postgraduate instruction provided by the medical faculty of Vienna.

Certain aspects of this large subject, such as the cardiac arrhythmias, congential heart disease, the acute endocarditides and pericarditis, are not included, but apart from this minor defect, the book deserves unqualified commendation. It is a model of condensed, clear and accurate statement and represents Wiener clinical medicine at its best. The section on "Treatment" shows the discriminating judgment and good sense that is evident throughout the book.

L. A. C.

APPAPEIL CIRCULATOIRE. By Ch. Laubry. Paris, 1935, Masson et Cie. 185 pp.

This work represents one part of the *Collection des initiations médicales* published under the direction of Dr. A. Sézary. It was designed primarily for the student, to serve as an introduction to the study of the circulatory system. In preparing the volume Dr. Laubry has accomplished the difficult task of selecting important points for emphasis, presenting his material clearly and concisely, and avoiding detailed discussions. By careful choice of material, omission of minor points, and condensation of style, he has provided an introduction to the study of cardiology which covers a wide field in a few pages.

E. H.

CONSULTATIONS DE CARDIOLOGIE. By Georges Marchal. (Collection du Médicin Praticien.) Paris, 1935, Masson et Cie. 228 pp.

In this volume we can visit Dr. Marchal's clinic and have presented thirty patients with various types of cardiac disease. The cases have been chosen to illustrate the types of heart disease which are commonly seen as well as several which are unusual: for example, a case of cardiac insufficiency occurring in the course of filariasis. The presentations are excellent with particular emphasis on the physical signs, and following each presentation is a discussion of the diagnosis, treatment, and prognosis. Dr. Marchal lays great emphasis on psychic and emotional factors in the production of symptoms, especially in the case of physicians who have cardiac disorders. He gives his treatment in great detail and is enthusiastic over the value of colloidal sulphur and streptococcus vaccines in rheumatic fever. He makes clear his general plan of management which includes rest, diet, psychotherapy, and drugs, but, while the general plan is clear, his use of drugs often seems arbitrary.

E. H.

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